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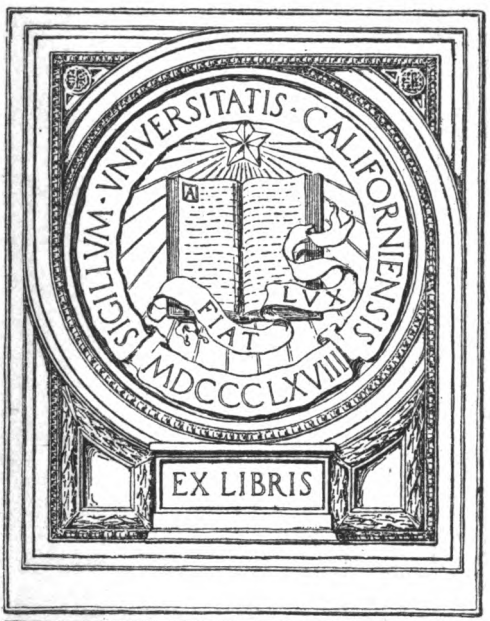
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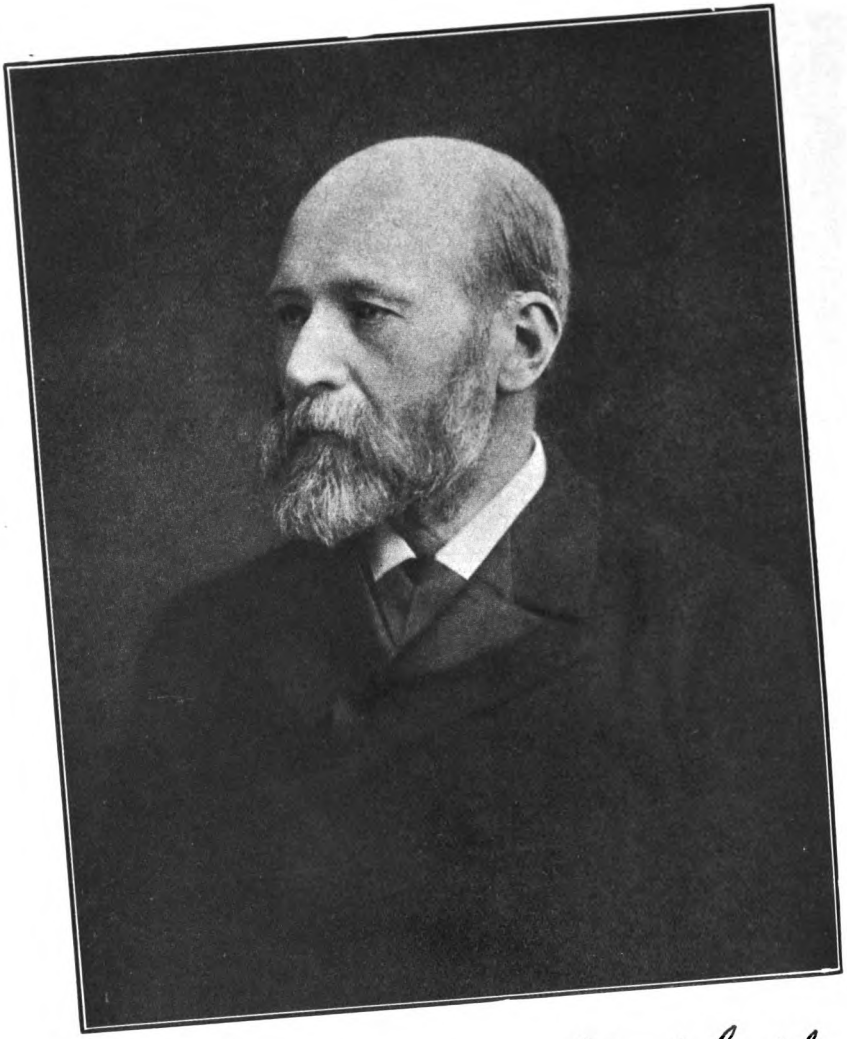


Yours faithfully
H. G. Howse.

In Memoriam.

SIR HENRY GREENWAY HOWSE.

Sir Henry Howse was a member of a family which had been for generations in Bath. His father, Henry Edward Howse, an only son, was never brought up to any profession, but was left well off, owning land and property besides the house, Lyncombe Hall, in which the subject of our memoir was born. His mother was Isabella Weald, the daughter of a merchant in London, and their marriage took place at St. Saviour's Church, Southwark, an interesting fact when we remember that Howse resided himself within two or three hundred yards of what is now Southwark Cathedral for something like twenty-five years. Henry Edward Howse was an ardent Unitarian, sometimes acting as a lay preacher. He was a very generous man, and presented several organs to Unitarian chapels; more than this, he brought up with his children some poor cousins, as well as the children of an Unitarian and others at various times.

Henry Greenway Howse was born at Lyncombe Hall, Lyncombe Vale, on December 21st, 1841; but soon after his birth his parents removed to Frenchay, a village about 4 miles from Bristol, and here in a house with a large garden in company with an elder brother, a sister, and the other children, most of whom were older than himself, he passed his childhood and early boyhood, until the age of fourteen. During this period he was educated at home by his father and one of his older cousins, and this rather irregular form of study was supplemented by Howse's own initiative in reading chemistry and physics from his elder brother's books, and by his devoting his pocket-money to the purchase of materials for experiments.

His school education began in September, 1855, when he went to University College School, then in Gower Street, near the College, and boarded with a family in the neighbourhood. His elder brother was at the same time in London training for the Unitarian ministry.

About this time their father moved to a house in Reading, where Mrs. Howse died a year or two later, when Henry Greenway was only sixteen years of age. At school he felt bitterly the want of a sound education in his earlier years; but he succeeded in taking prizes in physics and mathematics, and his subsequent career shows that he was well able to supply for himself what had been defective. On leaving school he returned to Reading, and was apprenticed to Mr. J. W. Workman, a medical man, from whom Howse learned a good deal, and of whom he always spoke with the greatest consideration and respect. Here, also, he must have read for the Matriculation Examination of the London University, for he passed it in 1859, taking honours in Chemistry. He was nearly twenty years of age when, in October, 1861, he entered as a first year's student at Guy's Hospital, contemporary with Sir George Savage, J. A. Ball, E. Coldridge Roberts, H. B. Spurgin, J. Milward, F. W. Humphreys, F. Manser, and the late Surgeon-general Skey Muir, S. W. Bushell, R. Eager, and H. C. Hilliard.

He soon showed his great capabilities. At the end of the first year he obtained the second prize for general proficiency and in his second year the first prize. In this year also, 1863, he passed the recently established Preliminary Scientific Examination at the University of London, and carried off the exhibition in Biology, so that in this summer he underwent successfully examinations in Anatomy, Chemistry, Physics, and Biology, showing distinguished ability in three out of the five. In this third summer, he exhibited even a greater capacity for covering a wide range of subjects, for he was first in hospital examinations which comprised Medicine, Surgery, and Midwifery, while at the University of London First M.B. examination he passed in Anatomy, Physiology, Materia Medica,

and Organic Chemistry, taking the Exhibition and Gold Medal in Physiology, including Histology and Comparative Anatomy, and Honours in Anatomy. There were few after his time who could raid at the same time the hospital prizes and University medals; for the school arrangements were made when apprenticeship was the custom, and a student might be expected to have a fair knowledge of practical medicine and surgery at the end of his third year, because he had learned much practice before touching anatomy and physiology. But the course of the University of London was not much different in its time-relations from what it is in the present day, and if a student straight from school passed the first M.B. (now the Second Examination for Medical Degrees) by the end of his third year, without knowing a particle of practical medicine, he was considered to have done well; as, indeed, he is now. Howse's success is partly explained, no doubt, by the industrious and honest use of his three years' apprenticeship, during which he certainly applied himself enthusiastically to the study of botany. What is so admirable, however, is his capacity for retaining so much diverse knowledge in his head at the same time, and producing it without confusion whenever he wanted it.

Two years later, in November, 1866, Howse passed the final M.B. Examination, taking Honours in Medicine and in Forensic Medicine, and the Gold Medal, that is, the second place, in Midwifery with marks qualifying for the Scholarship and Gold Medal, which were the reward of him who occupied the first place. This was the late Dr. Charles Kelly, who also took the Scholarship and Gold Medal in Medicine, a very able man who was one of the earlier prophets of sanitation and hygiene in England.

The next year Howse obtained the Scholarship and Gold Medal at the B.S. Examination, and again a year later, 1868, he became a Master of Surgery, obtaining only marks qualifying for the Gold Medal, but not the Medal itself. His rival on these two occasions, beaten by him in 1867, but beating him in 1868, was the late Mr. Marcus Beck, afterwards

surgeon to University College Hospital, whose memory is perpetuated in the Marcus Beck Laboratory of the Royal Society of Medicine. In 1868 also, Howse became a Fellow of the Royal College of Surgeons.

Needless to say, Howse was one of the most diligent men in the Hospital, and took in due course all the necessary appointments. He was dresser to the surgeon whose appointments were most in request, namely, Mr. John Hilton; he held also the post of Supernumerary Medical Officer in the Out-Patient Room, and he became House Surgeon in the spring of 1867.

In the following year he became a member of the teaching staff, being appointed Demonstrator of Anatomy, his colleagues being Mr. Bankart, Dr. Pye-Smith, and Dr. J. J. Phillips; and from that time onwards his connection with the School and hospital was assured, and it will be sufficient to say that he threw himself with his accustomed energy into all that he did, and passed through the usual grades as opportunity occurred.

He was in the dissecting-room three years, became Lecturer on Anatomy in association with Mr. Durham in 1871, and succeeded to the Lectureship on Surgery in 1888; this course he continued until his retirement. He became Assistant-Surgeon to Guy's Hospital in 1870 on the retirement of Mr. Hilton, and full Surgeon in 1875, when Mr. John Birkett was made Consulting Surgeon.

Mr. Arthur Durham had been in the habit of giving a short series of lectures on the use of the microscope. He was succeeded by Mr. Howse, who did pioneer work by starting a practical-class on the lines of present-day histology; and he continued to hold this class until a few years later. The profession then demanded that Physiology should be taught practically, as well as by systematic lectures, and a course of normal histology was accepted as the expression of this idea. The subject now became compulsory for every second year's student, and Dr. Pye-Smith took over the class. A separate class for morbid histology was subsequently added. When Howse

took the class in microscopy, the staining of animal tissues was in its infancy, and microtomes had not seen the light. The teacher could only bring the facts before his class by himself cutting all the sections with an ordinary razor, or, at most, one shaped for the purpose.

Howse was for a time also honorary secretary to the Pupils' Physical Society, and did much by his judicious guidance to further the aims and ensure the success of this valuable old institution.

About this time there were rapid changes on the surgical side at Guy's Hospital, and the entire Assistant Staff got command of the wards in less than three years. This was brought about by the retirement of Mr. Edward Cock and Mr. John Hilton in 1870 and 1871 respectively, and by the death of Mr. Alfred Poland in 1872. Mr. Cooper Forster, Mr. Bryant, and Mr. Arthur Durham were successively promoted as each vacancy occurred, and on the first of these occasions Mr. Howse became Assistant-Surgeon. Mr. Davies-Colley was appointed to fill the vacancy which occurred in 1871, but when in the following year Mr. Durham was moved up, the Governors decided not to make any further appointment, and thus Mr. Howse and and Mr. Davies-Colley acted for the following three years as the only Assistant-Surgeons, seeing out-patients each two days in the week, and assisting each of them two of the surgeons. They had thus exceptional opportunities for surgical practice. In 1875, on the retirement of Mr. John Birkett, Mr. Howse became full Surgeon with charge of beds.

As a lecturer and a teacher, and as a practical surgeon, Howse's characteristics were thoroughness in detail and a constant desire to improve upon existing procedures or methods. When a demonstrator he devoted himself to an effort to improve upon existing methods of preserving the subjects used for dissection. Probably no student or demonstrator in the present day can have experienced what those of fifty years ago had to go through in visions and odours as a result of the too rapid decomposition of the subjects. The agent of preservation was

a watery solution of arsenic injected into the arteries, and this was followed by the injection of red wax into the same vessels. Howse made use of glycerine as a fluid, which could be forced to permeate the tissues by injection through the arteries, which would not evaporate as does water, and which was in itself preservative of animal and vegetable substances in contact with it. He made numerous experiments by injecting limbs and portions of limbs, and he found that by this method the limb could be practically soaked in glycerine and that decomposition was absolutely checked. To make doubly sure he dissolved a small quantity of arsenic in the glycerine. That the glycerine soaked thoroughly into the tissues was shown by the fact that the arteries could be, after a certain interval of time, just as successfully injected with red wax as when a watery solution of arsenic had been used as preservative. I was a demonstrator of anatomy when this process was first adopted in the dissecting room and was in a position to judge of the enormous benefit which it conferred upon all those, whether students or demonstrators, who were working there.

Another undertaking of his should be mentioned, because it illustrates so well two essential points in his character—his desire to improve whatever he had to do with and his attention to detail. For some 9 or 10 years he was editor of the "Guy's Hospital Reports," and during that time he published eight volumes, the first of these by himself alone, the other seven in conjunction with the writer. So far as the scientific material of the Reports was concerned, nothing could have been better; but in all these ventures there is another side to be considered, namely, the commercial and financial. And the finance of the Reports had been allowed to get into a very complicated and unsatisfactory condition, having been entrusted to a dear old clerk in the Treasurer's office whose energies were probably too much engaged in the very big affairs of the Hospital estates to take much trouble about the Reports, and who, at any rate, was not in touch with old Guy's men, who form the bulk of subscribers to a work of this kind. Howse determined that it

must be the work of the editors to look after the finance as well as after the literary contributions. He started a complete system of account books to meet the special requirements of the publication, beat up the subscribers who had allowed themselves—or had been allowed—to fall into arrears, and thus brought to a maximum the financial support of the Guy's Hospital connection. Succeeding editors continued for a time the same system until, when the changed conditions of the affairs of the Hospital and School required a much larger staff of trained business men, it became possible for the editors again to relieve themselves to a very great extent of the purely business element in the Reports.

We have dealt so far with what may be called the diversions of the earlier part of his career. We may now come to the business of his life, that of a surgeon in hospital and private practice, and of a surgical teacher; and here I labour under a considerable difficulty, in that, being a fellow-student, though somewhat junior, I never myself heard his lectures or bedside teaching; and, being a physician, I am not in the best position to judge of his surgical qualifications. That he was successful as a teacher I know, from the large classes which he carried round with him in the wards, even on his regular Saturday afternoon visits. He had good and successful cases to show; he was keenly interested in everything bearing upon the cases, and he kept the student interested by constantly asking questions—surely the best possible method of teaching at the bedside. For many years his dressership was almost as much sought after as that of Mr. Hilton in former times. In his delivery of a lecture or speech at a debate he had acquired the unfortunate habit of constantly interrupting the flow of words by unnecessary interjections, so that he could never be regarded as a great orator; but this was not the result of any doubt or hesitation as to what he had to say—and, indeed, as a rule, he spoke rather rapidly in spite of the pauses. But here, as in other spheres of his activity, his complete knowledge of his subject, whether anatomy or surgery, his orderly

arrangement of it, the result of his careful preparation, his obvious enthusiasm and intense interest, were sufficient to attract and hold an audience to the full limits of the lecture hour. As a surgeon, Howse was cautious, deliberate, and even slow: and this characteristic it was which rendered him fittest to adopt the methods of Listerism, with their multiplicity of detail; but he was by no means wanting in boldness, as his initiative in excisions of the joints, in gastrostomy, and in the treatment of varicose veins abundantly shows.

Soon after completing his house-surgeoncy he studied in Paris, but, I think, only for a few months. A more important journey was that which he took to Edinburgh in order to study at first hand the antiseptic methods of treating wounds and operations which had been introduced by Lister, then Professor of Clinical Surgery, at the Edinburgh University. Howse threw himself whole-heartedly into all the minutiæ, and adopted in succession the various kinds of spray apparatus, which were then considered essential, and, indeed, were essential, for the confusion of the all-important germ. Fortified by these means he had no hesitation in attacking the joints of those poor sufferers from tuberculosis, whose only hope until then had been rest in bed for months or years, with the constant application of splints, assisted by Margate air and codliver oil. In the account given of Sir Henry Howse in the *British Medical Journal*, one of his colleagues, who was in those days his clerk or dresser, writes, "It was common to have as many as four or even six cases of excision of the knee under our care at one time. Howse superintended the dressing of every case, and must have spent the greater part of the five years of his assistant-surgeoncy in the Hospital. Failure in recovery was very rare indeed, and the large proportion of the knee cases had excellent and useful limbs. Had he published the results of this operation even in 1880, Howse must have taken a premier position amongst the surgeons of Europe at that time. No one could show so splendid a series of cases, not only from the point of view of mortality, but of usefulness of the limb."

Howse's material for work of this kind was obtained not only at Guy's Hospital, but also at the Evelina Hospital for Sick Children, which was opened in 1869, and of which he was appointed one of the surgeons in 1871. It was in the surgery of the abdomen more than in that of any other part of the body that the antiseptic methods had their greatest triumphs. The mortality from strangulated hernia, from intestinal obstruction, and from ovariotomy, was up to this date appalling, since infection and peritonitis were the sequelæ almost absolutely necessitated by the conditions then prevailing. Antiseptics gave the surgeons (and their patients) their opportunity, and Howse was one who grasped it readily. He was successful in his ovariotomies, not then handed over entirely to the gynæcologists; he operated successfully on an adult for intussusception; and he made gastrostomy a relatively safe operation in two stages, as is now constantly done. Another innovation of his was the treatment for varicose veins by excision. Of course, his practice was not confined to cases of this description; he dealt with the full range of cases which come into a surgeon's ward in a general hospital, or in a hospital for children; and to all he applied the same clear mind, careful consideration, and patient manipulations. For many years also he was surgeon to the Truss Society, and did his share of good to the public in this capacity.

Howse's retirement from the active staff became due, according to the Governors' regulations, in December, 1901. But the Lord Mayor, Sir Joseph Dimsdale, had consented that an appeal should be made at the Mansion House in January, 1902, for the public support of the finances of the Hospital, Mr. Howse was asked to remain in charge of the wards for a few months longer, and he spoke in support of the appeal in seconding the proposal of a vote of thanks to the Lord Mayor for his help on that occasion. In the succeeding March he was made a consulting surgeon, and retired from the active work at the Hospital. Howse was, of course, a Fellow of the Royal Medical and Chirurgical Society, and a member of the

Pathological and Clinical Societies; but he was not a frequent attendant at their meetings. He read papers before these Societies, but contributed nothing later than 1883, though he was an active member of a scientific committee of the Royal Medical and Chirurgical Society, which made a valuable report on the relations between membranous croup and diphtheria in the session 1878—1879.*

But Howse was not a voluminous writer in any direction: he did not take to the occupation kindly. He never published a book, and the only productions from his pen of a didactic nature are, first, the articles which he wrote for Heath's "Dictionary of Practical Surgery," (1886), on the following subjects: Injuries of the Chest; Rupture and Wound of the Heart; Wounds of the Lung; Hæmoptysis from Injury; Hæmothorax; Pneumothorax; and other special articles on injuries to the Chest; Femoral Aneurysm; Gastrostomy; Gastric Fistula; and, secondly, the articles on Hospital Hygiene in Stevenson and Murphy's Treatise on "Hygiene and Public Health," published in 1892. The remainder of his writings are mostly communications to the Societies already mentioned, to the Guy's Hospital Reports, and to the Medical Journals. But he gave the Bradshaw lecture at the Royal College of Surgeons in 1899, which was a review of surgery during the preceding century; and the Hunterian Oration at the same College in 1903. It was only in 1892, after he had been operating under antiseptics for more than twenty years, that he recorded his successes in the treatment of tuberculous joints, and of others requiring excision, to which allusion has been already made. The article is published in the Guy's Hospital Reports, vol. xlix., 1892, and occupies 106 pages. It is entitled "One hundred and thirty cases of excision of the knee, by H. G. Howse, M.S. The analysis of the cases by G. Newton Pitt, M.D."

Howse was always willing to take his full share of that work of management and organisation upon which the success of all

*Med. Chi. Trans., vol. lxii., p. 1.

institutions depends, and we see him rendering valuable assistance of this kind at his Hospital and School, at the Royal College of Surgeons, and at the University of London. At Guy's Hospital his opinion was much respected; he gave most earnest attention to the business, his judgments were only arrived at after careful consideration and were rarely other than thoroughly sound and trustworthy. One of the first things that Sir Cooper Perry did after he joined the Medical Staff of Guy's Hospital was to devise a method of acquiring a residential college, long talked of as desirable. Howse contributed to the success of this scheme by his useful counsels, and was no less concerned with most of the improvements in the School and Hospital which took place between 1880 and 1900. At the Royal College of Surgeons Howse was an examiner at different times. He was on the board of examiners in Anatomy and Physiology in 1883 and was on the court of examiners from 1887 to 1897. He was elected a member of the Council of the College in 1889, and was re-elected in 1897 for another eight years, retiring in 1905. In this later period he was Vice-President from 1897 to 1900, and President for two years, being elected to that office in 1901 in succession to Sir William McCormac, and being succeeded by Sir John Tweedy in 1903.

He had previously been Acting President, when Sir William McCormac went to the South African War. I am informed by Sir Rickman Godlee, who was then a member of the Council, that Howse discharged the duties with great efficiency, though, as a matter of fact, there were no striking occurrences during the time he occupied the presidential chair. As an examiner, both in Anatomy and Surgery, he gained a reputation for thoroughness and fairness, both from his colleagues and from the candidates.

It was in 1902, during his tenure of the Presidency of the College, that he received the honour of knighthood, much to the delight of the whole of his Guy's Hospital friends.

The honorary degree of Doctor of Science was also conferred upon him by the Victoria University, Manchester.

Sir Henry Howse was an active member of the University of London, so far, one might say, as one could be active in the old University before its reconstitution. The Senate was not a representative body, and outside its own committees and sub-committees the only advisory body was Convocation, which consisted, as now, of all graduates of the University who are willing to pay a small fee. They number now between eight and nine thousand. Any member of the Senate, also, is *ex officio*, a member of Convocation. Convocation elected a committee, called the Annual Committee, consisting of representatives of the four faculties—Arts, Law, Medicine, and Science, and this committee discussed matters of high university politics, of which reports were laid before Convocation, and upon which Convocation reported to the Senate, after full-dress debates and important divisions. Guy's Hospital was represented on the Annual Committee, Dr. Hilton Fagge and Dr. Pye-Smith being members for many years. And prominent in the debates in Convocation were Mr. Farrer Herschell, later Lord Herschell, Mr., now Sir, Philip Magnus, and Member of Parliament for the University, Dr. Fagge, Dr. Pye-Smith, Mr. Hutton, the well-known editor of the *Spectator*, and others. But the general impression in Convocation was that its recommendations were not regarded very seriously by the Senate.

Howse did not take any prominent share in this phase of University life, but he was in favour of promoting communication between the various elements in the University, and he was, for a number of years, honorary secretary to the University Dining Club, which was open to graduates in all the faculties and met several times in the year for discussion, over an inexpensive dinner, of the affairs of the University. In due course Howse became examiner in Surgery at the University, and when the University was reconstituted in 1900, and the Senate was built up on a representative basis, Howse became one of the two representatives of the Royal College of Surgeons, and served for five years. It was during the first three or four years of the University's new career that the examinations in the medical

faculty were overhauled. Up to that date, with the exception of the introduction of the Preliminary Scientific Examination in 1861, there had been very little change in the scheme of the medical and surgical tests. But in the last few years of the nineteenth century a committee of the old Senate, under the presidency of the Vice-Chancellor, Sir Henry Roscoe, was considering the whole subject, and in this work Sir William Allchin, Physician to the Westminster Hospital, and at that time Examiner in Medicine, took an active part. But the reconstitution necessarily delayed the matter, and we may suppose that when it was brought up again before the new Senate, Sir Henry Howse would have had a considerable voice in approval or otherwise of the new scheme. Howse was much interested in the higher education of women, and was for some years on the Council of Bedford College. He was an early supporter of the admission of women into the medical profession.

The impression that Howse must always have given during his studentship and earlier years on the Staff was that of an indefatigable worker, living within a few yards of the Hospital, regular and punctual in his engagements, carrying through every bit of work in the most thorough and painstaking manner, and really splitting the night's rest into two parts, with a large interval of work between them. Athletics, in the ordinary sense of the term, did not interest him, or, more probably, he would not give the time to them, for as a schoolboy he had been very fond of cricket, and was a good player; and later he developed activities, of which more presently. But he had recreations of other kinds in great number.

He was fond of music, played the piano, and had made the personal acquaintance of the more familiar operas and oratorios. He purchased a turning-lathe, started a workshop, and spent many an hour in this absorbing occupation, which he found useful in the repair of toys when his young family had learnt how to break them. He was fond of chess, and took it seriously, learning his gambits with great conscientiousness; he could play a fair hand at whist; he was always interested,

in botany, and had made a collection of dried plants. He was also a good reader and had a good library of classical works, both English and French. He had a taste for gardening, but he was hardly able to carry this out until he took a residence in the country; though the writer remembers that in St. Thomas's Street, in his bachelor days, he at one time invaded a piece of ground, which was easily accessible from his house, apparently entirely derelict, and for a time carried on amateur gardening operations therein. However, one day, somebody having prior rights over his land of promise, appeared on the scene, and the gardening programme had to be postponed indefinitely.

In the country, however, Howse was able, like so many who retire, to develop and enjoy his bucolic tastes. He took, indeed, a great deal of pleasure in the nurture of his plants and added to it the care of an engine and the rest of the electric lighting plant which he installed in his new home. Photography and, in his later years, croquet were additional means of passing the time, when professional occupations failed him. But the recreation which had the most fascination for him as a young man, and even up to his fifty-fifth year, was that of mountaineering, the practice of which was, of course, restricted to the summer holiday. I was fortunate in being his companion on six of these annual excursions to Switzerland, and we habitually climbed without guides. This practice was in those days comparatively rare, and was rather discountenanced than otherwise by the Alpine Club. When I first joined Howse in 1875, he had already done much climbing in Switzerland with and without guides; and had learned much of the art and science of it in company with his elder brother, the Rev. E. S. Howse, and on one or more occasions with Dr. R. Eager. He was well versed in the literature of the subject, was familiar with Ball's "Alpine Guide" and Girdlestone's "High Alps without Guides," and he scarcely got back from one holiday before he was plotting the campaign for the next. More important than all this, I can say that Howse was a most careful and prudent guide, always providing as far as he could for every contin-

gency, never leaving anything to chance that could be brought within the range of certainty—some things in mountaineering cannot—always prepared to give way, or to renounce a peak, or a pass, if the weather or the local conditions should prove to be too strongly adverse. We certainly had most enjoyable holidays.

If we did not climb quite such big things, or do them so fast, as those with guides, and if we had to carry our own food, perhaps enough for thirty-six hours, and our sleeping bags, we still had the compensating pleasure of independence of action, of accomplishing the deeds ourselves instead of being led like sheep, of stopping or of going at our own pace, and all the credit of success in a difficult or troublesome undertaking. I must not be misunderstood about the sleeping bags. We carried them, indeed, but they were very light. The bag was devised by Howse, and made by ourselves, of thin mackintosh cloth, in double layer, so that it could be blown up with air after the would-be sleeper was inside. When the bag was empty, our baggage was wrapped up and strapped in it, so that it took the place of a regulation knapsack or rücksack. A seventh Swiss tour in company with Howse was denied me in consequence of his entering the bonds of holy matrimony; but he continued his alpine vacations, in Switzerland or in the Tyrol, for some fifteen years more with his new companion. Carrying knapsacks, rope, and ice axes, they climbed, often without guides, and had a few adventures and even some narrow escapes.

For a great part of his student life, and during his first two years as a teacher on the Staff of Guy's Hospital, Howse lived in a single bed-sitting-room in Great Maze Pond. For some years his father's affairs had not been so satisfactory as formerly, and Howse was content to live economically. But when he was appointed an assistant-surgeon, and Mr. Cooper Forster moved to his new house in Upper Grosvenor Street, Howse took the vacant house in St. Thomas's Street, which was then No. 10, but is now No. 24. This was one of the two, com-

paratively recently built by Guy's Hospital, and leased to Dr. Braxton Hicks and Mr. Cooper Forster as the first tenants. Here he remained several years. Not even five years residence in the Borough, nor his promotion to the full Staff at the end of that time, induced him to set up a brass plate in the west end too soon. I have no doubt that the advantages of proximity to the hospital when he was devoting himself to all the work which the Listerian methods involved, were for him a good reason why he should be contented with his lot; while he, no doubt, early began to be consulted in surgical cases arising in the south of London. At any rate, it was not until twelve years later, namely, in 1887, when he had already set up a carriage and pair, and married, that he transferred himself to the west end, taking a large house, No. 59, Brook Street, where that street is crossed by Davies Street. Here he practised until 1903, when having retired from the Presidency of the Royal College of Surgeons, he took the "Tower House," at Cudham, in Kent, situate on a considerable eminence over against Down, where the great Darwin resided for so many years and died. Howse kept up his connection with town for some three years longer, and had rooms at 22, Grosvenor Street, where he was in the habit of seeing patients about three times a week.

Howse did not lay himself out to make acquaintances, but those who knew him long enough had the staunchest of friends. Though not given to writing or eager to speak in public, he had a large fund of information, was extremely keen to get knowledge on any subject, and his conversation was always interesting and instructive. Moreover, he was always prepared to see the humorous side of things. Living as I did within a few doors of him for more than a dozen years, I was constantly consulting him on matters of School and Hospital in which, as Dean, I might have been anxious or desired assistance. Of course, he helped me, but more than that, I always knew that he would give the matter the fullest and most careful consideration; and always the right advice was forthcoming.

When I look back upon those occasions I cannot recall a single occasion on which his opinion could have been said to have been influenced by a thought of his own welfare, or on which it was not wholly and entirely formed in the interests of others or in the common interest of the School or Hospital. Nor can I remember him to have expressed or entertained any unfriendly feeling or other than a kindly sentiment towards any of his acquaintance.

Howse was nearly forty years of age when he married Alice, the youngest daughter of the Rev. T. Lethbridge Marshall. Their family consisted of three daughters and one son; but the eldest daughter, to their great grief, died in her twentieth year. Howse was very rarely away from his work on account of ill-health. When house-surgeon he suffered from a severe and rather long attack of jaundice, but continued his work in spite of it. Later on, but still early in his career, he had a bad septic wound of one forefinger, which remained stiff ever after. With these exceptions, and occasional catarrhal attacks which often extended to his chest, laying him up for a few days, he was well until about the time of his retirement. Then in the first year of his residence at Cudham he had pain in the thigh of the nature of sciatica, followed by osteo-arthritis of the knee, and probably ostitis, which made locomotion difficult and troublesome, and considerably hampered his enjoyment of life. Accordingly after a time, indeed for the last eight years of his life, he kept himself very much at home, less and less often came up to London, especially after the termination of his Presidency, and grew to dislike travelling in any way whatever. He devoted himself to gardening, to the care of his poultry, and to the management of his electric plant and engine, interested himself in his children's studies and occupations, and followed closely their wanderings when they paid visits in England or abroad. Always a great reader he continued this in his later years, especially in history, biography, French, and some German, and helped in philanthropic movements in the little village in which his estate was situated. Thus time slipped away, but the trouble

in his limbs increased to a serious extent, and extensive structural changes were obviously taking place, as he lost in stature much more than his years alone would account for. Ultimately he suffered intense pain and gradually became exhausted, sinking to rest on Tuesday, September 15th, 1914. The funeral took place on the following Saturday at St. Luke's Cemetery, near Bromley. Howse himself maintained his connection with the Unitarians, and attended Stopford Brooke's Chapel.

Howse was short of stature, but thick-set and strongly built, and capable of great endurance, as was manifest on his alpine excursions. He was early bald, and his well-formed head and aquiline nose gave the impression of great intelligence, while his clear blue eyes frequently twinkled with suppressed humour. He wore a full moustache and beard; the severe principles of asepsis had not yet, while he was in practice, driven all trace of hair from the faces of our surgical colleagues. He had just that convenient degree of short sight which, while not compelling the constant use of glasses, postpones the need of them in old age.

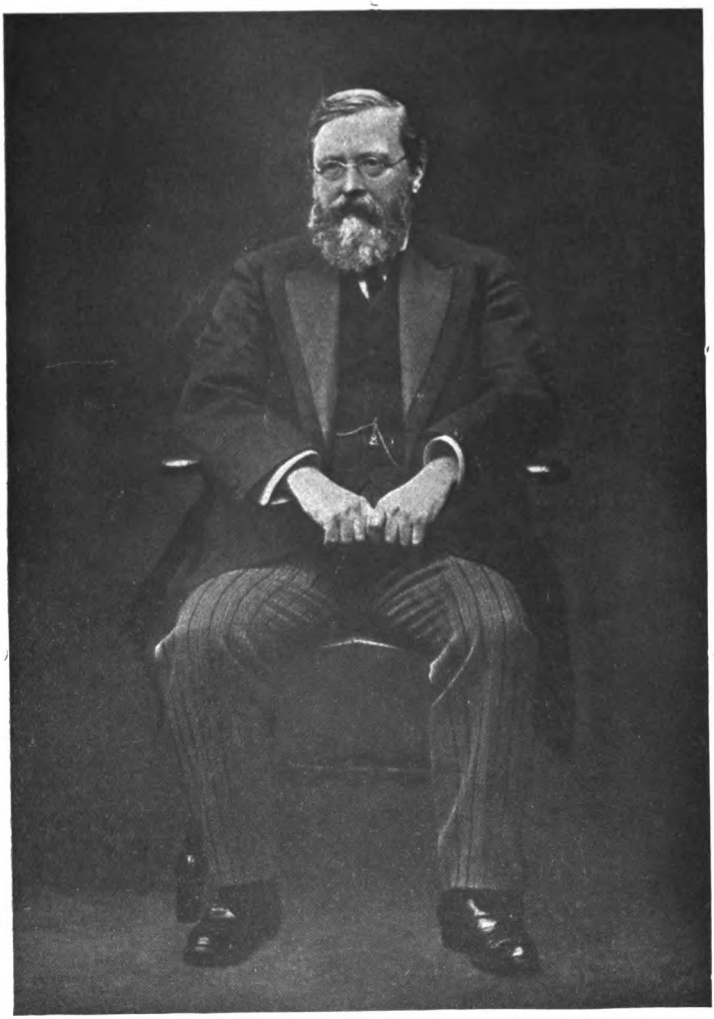
A portrait in oils of Sir Henry Howse hangs on the staircase wall of the Court Room of Guy's Hospital. It was painted by Mr. Lance Calkin in 1903 when Sir Henry was 62 years of age, and may be accepted as a good likeness.

The portrait which accompanies this memoir was probably taken in the year 1902, on his retirement from the active Staff of the Hospital.

Howse wrote no kind of book; but he will live in the annals of the institutions which he has served; and by his colleagues, his personal friends, and his pupils, he will be remembered for one of the ablest, justest, and best of men, to the end of their time on this side of the dark flood.

FREDERICK TAYLOR.

UNIV. OF
CALIFORNIA



Yours Faithfully
P. Horrock

In Memoriam.

PETER HORROCKS.

It is always felt to be an interesting fact in the life of a distinguished man that his life's work should have been foreshadowed by his tendencies in boyhood. But it must be allowed, I think, that in a great number of instances no such premonitions of a career can be recognised. Numbers of boys are determined as to their future by the professions or occupations of their fathers, and if they follow such occupations in adult life with success, it is, may be, not because they had any particular liking or capacity for them, but because they were boys or men of average ability and industry, and would have taken as readily to any profession which offered. In some of the biographies of Napoleon it has been stated that he was successful in his schoolboy pugnacity, and, on the other hand, in some of those of Wellington it is said that he was not. Here and there, in a school, a boy may show a desire to become a doctor; more often, perhaps, to be a clergyman; often one hears of the wish to minister to the sick having been created by a severe illness in which the boy has been a witness of and has been benefited by the skill and sympathy of his medical attendant.

But with the exception of the profession of fighting, whether on land or on sea, probably very few occupations or professions are sufficiently understood by the middle-class schoolboy to attract him to one or the other. And the selection of a profession does not at once settle the question of what exactly the student will eventually do.

The law student may specialise in various directions: the barrister has the choice of different branches, or may take up

literature or journalism, the medical student may become a physician, a surgeon, a general practitioner, a health officer, or a radiographer; may confine his treatment to or profess a limitation to one part of the body; or may devote himself to state medicine; and probably at the commencement of the curriculum he has not made up his mind to which line he will take.

Certain it is that many men, who have appeared to be destined to a satisfactory, if not brilliant, career in one branch of the healing art, have ultimately dropped into, and made a solid reputation in, quite another. I could, I think, give instances where men who seemed marked out as physicians have for some reason or other taken to surgery. I remember striking illustrations from the roll of obstetric physicians.

The late Dr. Galabin had certainly all the makings of a pure physician; and on his arrival at Guy's as a medical student, with a brilliant career as a mathematician behind him, I think everyone must have formed the opinion that he was better fitted to deal with the obscure problems of medicine than to practise the manipulations which characterise surgery; or, to put it in another way, that, to the involved problems of medicine, he was likely to worry out more answers than most men of his time. And, indeed, before he was appointed a member of the Staff, he did a most valuable piece of physician's work in studying with the cardiograph the movements of the heart in disease: and he wrote an original paper on it, which is occasionally quoted even in the present day. But one morning in January, 1874, when London was wrapped in one of the worst of its bad fogs, we learned that Dr. John Jones Phillips, our genial and popular Assistant Obstetric Physician, had been found unconscious in his bed that morning, and within a few hours was dead, from cerebral embolism following heart disease. The obstetric staff was then practically limited to the Physician and the Assistant Physician. Dr. Braxton Hicks was little more than fifty years of age, and a vacancy was quite unexpected: Dr. Galabin's application for it was conceded by the Governors. I need not say how well he rose to the occasion; how he wrote really

popular text-books both on Obstetrics and on Gynæcology; or how he applied his mathematical genius to the problem of how the fœtus manages to thread its way from the brim of the pelvis to its outlet, without being hopelessly stuck fast in the process.

Mr. Targett can scarcely have made an Obstetric Physiciancy or Surgeoncy his first aim in life; for, by the time that he had taken his higher degrees, the two posts at Guy's were held by men comparatively young, Dr. Galabin little more than forty, and Dr. Horrocks only thirty; so that, in the ordinary course of events he could not have expected to succeed in less than seventeen or eighteen years. His bias towards surgery was shown by his taking the London University B.S. Degree, the Fellowship of the Royal College of Surgeons, and the London University M.S. Degree, in successive years, at a time when he was occupied as Surgical Registrar. During the succeeding ten years he was Demonstrator of Anatomy, and later Demonstrator of Surgical Pathology at Guy's Hospital, while almost simultaneously he was Pathological Assistant, and later Curator of the Museum of the Royal College of Surgeons. Only at the expiry of this time did Mr. Targett become, at the age of 35 years, specially associated with Obstetrics and Gynæcology, when in 1897 he was appointed to the new post of Obstetric Registrar and Tutor at Guy's Hospital. He thus became an assistant in the department controlled by Dr. Galabin and Dr. Horrocks, whom in due course he succeeded.

It is interesting that the subject of the present memoir should be another instance taking an intermediate position in time, between Dr. Galabin and Mr. Targett. It will be sufficient here to point out that Dr. Horrocks was Physician to Out-Patients at the National Hospital for Paralysed and Epileptic, when his thoughts and work were turned in an entirely different direction by the occurrence of a vacancy in the Obstetrical Staff of Guy's Hospital.

Peter Horrocks was born on February 21st, 1853, at Farnworth, near Bolton, in Lancashire. He was the seventh son of

George and Ann Horrocks, and his father was a cotton-spinner and manufacturer.

His education was first undertaken by a Mr. Henry Knox, but he afterwards went to Farnworth Grammar School, and subsequently to the Owens College, Manchester. He studied here for three years before coming to London, during which time the professors included Sir Henry Roscoe, Balfour Stewart, Stanley Jevons, Dr. Ward, now Master of Peterhouse, and others well known in the scientific and literary world. At Owens College he obtained a classical prize of some value, given by the late Professor Wilkins; and in January, 1872, while still at the college, he passed the Matriculation examination of the University of London, being placed 27th in honours. In the following year he passed the combined Intermediate Science and Preliminary Scientific (M.B.) examination, and entered at Guy's Hospital in October, 1873, being then well on in his twenty-first year. Among his contemporaries were Henry Davy of Exeter, W. F. Hearnden of Sutton, Sir Arbuthnot Lane, Dr. J. W. Meek, Mr. A. E. Maylard, Professor of Surgery in Glasgow University, the late Sir Robert Simon, and Dr. Uhthoff of Brighton. He threw himself into work, having as his object the Hospital prizes and the degrees of the University of London. Thus at the end of his first year he obtained the third prize, value ten guineas, for general proficiency; the first prize was taken by J. W. Meek, the second by Henry Davy.

In his second year he passed the 1st M.B. Examination of the University of London, and obtained Honours in Physiology.

In his third year he obtained the second prize for general proficiency, the subjects being then those required in a final qualifying examination, namely, Medicine, Surgery, and Midwifery. The first prize was taken by G. A. Wright, now Emeritus Professor of Surgery in the Victoria University, Manchester.

In the summer of his fourth year, reading as he was for the Final M.B. Examination, he secured the Treasurer's Gold Medal for Clinical Medicine. In the same year he became a Bachelor

of Medicine. It was a matter for debate then, as, I dare say, it is now, whether it is better policy to go in for the Final M.B. before undertaking House Appointments, or after having had the valuable experience associated with them. In accordance with, if not in consequence of, my advice, he went in for the examination at the earliest opportunity, his knowledge based upon authority, uncomplicated by the distortions it was likely to suffer in the first months of independent judgment and action. He not only succeeded in passing, but he obtained the second gold medal in Medicine, with marks qualifying for the scholarship. He also took honours in Obstetric Medicine. In December of the following year, 1878, he took the M.D. degree; and then went abroad to continue his studies in France and Germany. In Paris he studied under the great Charcot, whose clinical teaching on nervous diseases at the Salpêtrière was attracting crowds of students and graduates from all parts of Europe and America. In Germany he went to the University of Würzburg. Here he worked under Professor Rindfleisch, whose excellent text-book on Pathological Histology was widely read in Germany and had been translated, both in England and the United States. Horrocks worked hard with the microscope: he also attended the clinique of Professor Gerhardt, and on coming home he told the writer with much satisfaction how the Professor on one occasion quoted to his class a recent paper in the Guy's Hospital Reports on the use of copaiba resin as a diuretic, and forthwith ordered this medicine for the patient.

Returning to England, he was in 1879 appointed a Demonstrator of Anatomy, at that time still the first rung of the ladder for nearly all the Physicians and Surgeons. In the following year, seeing no opportunity of exercising himself in the practice of medicine at Guy's Hospital, he applied for the post of Assistant Physician then vacant at the National Hospital for the Paralysed and Epileptic in Queen Square, and was elected. About the same time he was entrusted with the management of the Electrical Department at Guy's Hospital. And so for three or four years he was engaged in teaching Anatomy at Guy's,

and in the study and treatment of nervous diseases at the National Hospital, as well as at Guy's. In this interval he took a good deal of trouble about an article for the Guy's Hospital Reports, into which he put his best efforts, with the feeling, as he expressed it to the writer, that it was desirable that anything he published at that time should be thoroughly well done. The article is entitled "Reflex Action in Diagnosis," and occupies 39 pages of the Reports.* The subject was comparatively new: only three years previously had Prof. Grainger Stewart, of Edinburgh, and Dr. Thomas Buzzard, in London, brought to the notice of the medical profession in England the work of Erb and Westphal in relation to the patellar-tendon reflex, or knee-phenomenon; and Sir William, then Dr., Gowers, in 1879, had read a paper before the Royal Medical and Chirurgical Society on the so-called tendon reflex phenomena, namely, the knee-reflex and ankle-clonus. Horrocks dealt fully with all the reflexes: those of the skin and mucous membranes, those of the muscles and tendons, and those of the special senses. He supported his arguments by means of original experiments, and by notes of cases from his out-patient practice at the National Hospital. It was a thoroughly good piece of work.

In 1883 the crisis of his career as a physician came. Dr. Braxton Hicks in the spring of that year reached the age which the Governors had adopted as the limit of service on the active staff, and the rule took effect. But there was no under-study in the Obstetric Department. Obstetric Registrars had not been invented: and nobody seems to have realised that a vacancy was imminent. There is reason to believe that even Dr. Hicks himself thought that he would go on for another year. The Governors, after their little differences with the Medical Staff scarcely more than two years previously, might well have taken the opportunity to throw the appointment open, and to invite applications from all and sundry by notice in the medical papers. Happily they

* Guy's Hospital Reports, Series 3, vol. xxv., 1880–1881, p. 51. From internal and other evidence it is clear that the article was finished about Midsummer, 1881.

were content to receive tenders from Guy's men only, and Dr. Horrocks was appointed. Could he have known what was in store for the Medical Staff of Guy's Hospital, could he have foreseen that death would have been so busy in a few years, and that his junior in the dissecting room would be full Physician with beds in less than seven years, he might have been content to wait. But these things he could not know; he could only see that Sir Samuel, then Dr., Wilks was due to retire in about a year and that Dr. Carrington was marked out by his great abilities and conspicuous industry to come on as Junior Assistant Physician—and then apparently a long wait. Horrocks started on his new career. With characteristic energy he threw himself into the work.

Recognising that his experience of Obstetrics and Gynæcology was somewhat limited, he obtained leave of absence, and went to study at the Rotunda in Dublin.

At the time that Horrocks abandoned pure medicine to become an obstetric physician, the movement had already begun amongst gynæcologists to perform for themselves those surgical operations in connection with the female pelvic organs which they had been bound by custom, and by the rules of their Hospital, to hand over to the surgeons. Dr. Galabin, his now senior, was a strong advocate of the desirability, the justice, and, he would have said, the necessity, of this step. And, indeed, at Guy's Hospital the surgeons had already conceded the right of the chiefs of the Obstetric Department to perform their own operations; and the Governors had assented to this transference of responsibility from the Surgeon to the Gynæcologist.

Horrocks was, therefore, from the first an operating obstetric surgeon, and thoroughly prepared himself for all the duties devolving upon him in that capacity.

He joined the Obstetrical Society and took an active part in its debates, showing one or two specimens in every session, and frequently joining in the discussions. He acted as Honorary Librarian for the years 1888 and 1889, as Honorary Secretary from 1890 to 1893, as Vice-President in 1895 and 1896, and he

occupied the Presidential chair in 1901 and 1902. After 1905 his contributions to the debates were much less frequent. In 1907 the Obstetrical Society became the Obstetrical Section of the Royal Society of Medicine; and Horrocks in December of that year made his last contribution to the section.

Though a regular attendant at the Society, he has left little behind him in the form of contributions to obstetrical science. Some of his clinical lectures are published in the "Guy's Hospital Gazette." The first fully reported lecture is in the volume for 1902, and the subject is "The Modern use of the Curette." In 1903 he became Senior Obstetric Physician by the retirement of Dr. Galabin, and lectures appear by him in successive volumes on "Sterility," "Two Cases of Pyo-salpinx," "Myomectomy," and "Ovaritis." In the Guy's Hospital Reports for 1885-86 he had a practical paper on "Uterine Dilatation," illustrated by cases. Personally, I had few opportunities of forming an opinion as to his professional capabilities, whether in the wards, in the operating room, or in the lecture theatre.

Mr. Bellingham Smith, who was his colleague and has eventually succeeded to his post in the Obstetric Department of Guy's Hospital, has kindly supplied me with the following appreciation of Dr. Horrocks :-

"He was an interesting teacher and lecturer. I believe his lectures were illustrated and pointed throughout with apposite and often entertaining tales of cases. You know how amusing he could be. His teaching was simple and clear, and what it should be for students, and for that matter for anyone interested in the subject; not overladen with detail, but the main points brought out clearly in his slow, north-country speech, and brought out in such a way that they and perhaps some appropriate anecdote remained in the memory. It was the same with his clinical teaching. He was admirable in the way he impressed students with the importance of salient points. I remember him looking over his glasses, with his eyes wide open, at a student who had proposed to cut off the arm in a transverse presentation, and saying to him slowly and impressively,

and wagging his forefinger close in front of his nose, 'That's awful.' I do not suppose the student ever proposed again that line of treatment. In this sort of way he knocked a few facts into men.

"His clinical knowledge was, I believe, based almost entirely on experience and not on the writings of others. I have an opinion that he read but little. It was always with him, what 'I have seen,' what 'I have done,' never what he had learnt from others: or, at all events, that is the impression I have carried away with me. The consequence was that his teaching was almost entirely clinical: the symptoms and treatment of a case, the pathology seldom, and that but slightly touched upon and often wrong.

"He was undoubtedly good in his clinical work. He had a retentive memory, and he always had a store of cases to fall back upon. He was a shrewd judge of human nature, and this with his considerable experience and his good memory made his judgment in a case a sound and valuable one.

"If there was one feature more than another that one would point to as distinguishing him, it was common sense. As far as I know he had no fads. Perhaps new lines of treatment were not so common a few years back as they are now. At any rate, I do not remember that his treatment was ever marked by anything but sound commonsense, such treatment as would lead to the recovery of the patient rather than to his own glorification. It was the same with papers that he read. They were on the subjects of everyday practice; the management of a case of labour, or of a lying-in woman; and yet they were points of the greatest importance which he insisted upon. I believe he was one of the first to insist on the uselessness, and the danger even, of douching in the lying-in stage of labour. Looking back, one would almost say he preached the obvious; only the obvious was then so opposed by routine that it was difficult to grasp.

"Perhaps it was simplification of treatment that appealed to him. Having that instinct strongly ingrained in myself, I seem to see it and feel it in him. One feels that the over-elaboration

of ritual in operation was foreign to him. This leads too often to slowness, and he was a quick operator. He would not be counted among the brilliant operators, such as was Durham in the past, but one felt that he was all the time putting in good work, wasting no time, and not playing to the gallery. An operation he loved performing, more common nowadays than it was then, was Cæsarian section. He liked an audience for this, and he would always give a little lecture on the subject beforehand. It was, and is perhaps still, a gallery operation, and who is free from the love of occasional display, the thrill of the baby coming suddenly into the world through its mother's abdomen being ever present, both with operator and spectator.

"I do not think that he gave his name to any new operation. He employed for the induction of premature labour a thin rubber bag to which he gave the name of Maieutic. This, I confess, I have not much used, owing to the difficulties entailed by the rupture of the bag; but Dr. T. G. Stevens uses it and speaks well of it.

"Horrocks was always kind to his poor patients. He was a very human man in his dealings with patients, and in his life generally, as I see him, a man of much vitality, with strong likes and dislikes, and perhaps difficult to work with."

Horrocks enjoyed a considerable private practice. While he was Demonstrator of Anatomy he lived at 29, Merrick Square, the rather desolate little encampment half a mile south of the Hospital. At about the time of his appointment on the permanent Staff he took one of the houses in St. Thomas's Street, which have sheltered so many of the Guy's Hospital Staff. This was the house numbered 9, adjacent to the Hospital; it became 26 when the street was re-numbered in 1889. Here he was the only representative of the Obstetrical Department of Guy's Hospital resident in the south of London, and he was certain to be called in to many cases of obstetrical emergency in the large south-eastern district. It was not till 1896 that he moved to the west end of the town, tied, no doubt, to the neighbourhood of the Hospital by the requirements of the Guy's Hospital Ma-

ternity Charity, in the working of which he was the final appeal in difficult cases. However, in the year stated he took the house No. 45, Brook Street, Grosvenor Square, where he resided a few years, and then moved into No. 42, on the opposite side of the street.

Horrocks had a keen sense of enjoyment. He never took a gloomy view of life. A hard worker in his profession, he was also very fond of physical exercise; and though he may have been fully alive to its value as a means of keeping off the demon of corpulency, I never heard him give that as a reason for his activity, and the pure enjoyment of it was, I believe, the stronger motive.

In the early days of his residence in St. Thomas's Street the safety bicycle had not been discovered, and Horrocks would occasionally on a summer evening take train to the south of London, hire a tricycle, and have a run of twelve or fourteen miles. A boat on the river on Sunday was another way in which he relieved his tension, and got rid of the cobwebs. In later life he took to mountaineering in Switzerland, and here he had an exceptional experience, which nearly ended disastrously for him, as, indeed, it did for one of his guides. It was in 1894. He had climbed the Zinal Rothhorn with two guides, and on the way down they were traversing the well-known ledge of rock not far from the summit. This ledge is from ten to fourteen inches wide, has a wall of rock on the one side, and on the other the rocks fall away almost sheer for a distance of a thousand feet or more to the glacier below. His first guide had passed along the ledge, and was drawing in the rope as Horrocks was feeling his way along. The second guide was behind him at the far end of the ledge paying out the rope. The first guide was bearing with his foot against a mass of rock, which, he said, had been treated similarly by the guides for years. But on this occasion the mass of rock gave way before the guide's pressure; he fell 60 or 70 feet, but came down on his feet in a mass of soft snow. Horrocks was pulled off the ledge, but by a merciful chance one part of the rope, which

was knotted behind his back, caught on a projecting piece of rock, not so far below the ledge; and Horrocks was hung up with his back against the rock, and, happily, in an upright position. The second guide was also pulled out of his steps, and was flung through the air. When the rope became taut between him and Horrocks, it snapped, and the unfortunate guide fell on to the glacier below, and was dashed to pieces.

Horrocks, finding his hands free, felt his pulse, and found that it had about the normal frequency; and though shaken, he felt that he was not seriously injured. Happily there was another party on the mountain coming down a little distance behind him, a gentleman and his wife and their two guides. Before Horrocks had been long in his critical position, the guides were able to haul up his surviving companion, and then he himself was pulled up on to the ledge, and a safe descent was effected. For many a man who had gone through such an ordeal that day would have seen the end of his mountaineering. Not so with Horrocks. He was in Switzerland the next season, and though I do not think that he went to the playground of Europe regularly every year after that, he certainly went sometimes, and, I believe, he was climbing thirteen or fourteen years later, shortly before the year in which he died.

Horrocks was fond of travelling apart from climbing. At one time a brother was resident in Finland, and Horrocks sometimes paid him a visit. He also went to the United States, and I remember well his telling me, on the eve of his departure on one such occasion, that he regretted it looked as if the weather might be very fine, as he much preferred a boisterous passage.

As far as I remember Horrocks mostly had good health, and I cannot recall any serious interruptions of his work until his illness in the year 1907. It was in the summer of this year that he had the first indications of vesical trouble. After some months it was obvious that an operation must be done, and some growth was removed in December. By the end of February, 1908, he had returned to work, but the recurrence of symptoms in the early summer showed that he was not out of danger.

Indeed, the local condition became more and more threatening, and his health was in other respects not satisfactory. In February, 1909, another operation was performed, but he succumbed a few days later, on February 28th, seven days after the completion of his fifty-sixth year.

Horrocks was never married. He was of middle height, powerfully built, and put on weight as he grew older, without ever being corpulent.

The portrait which accompanies this memoir is in all respects excellent. It illustrates his cheerfulness and geniality and equable outlook upon life. In the Medical School Buildings of Guy's Hospital is a bronze bust of him, which was presented to the School by his brother, Mr. Walter Horrocks, of Darwen, and was unveiled by the Treasurer, Viscount Goschen, in November, 1910.

FREDERICK TAYLOR.

WILLIAM ARTHUR BRAILEY,

OPHTHALMIC SURGEON TO GUY'S HOSPITAL,

1882—1905.

DIED APRIL 8TH, 1915.

In Memoriam.

WILLIAM ARTHUR BRAILEY,

M.A., M.D. CAMBRIDGE.

Consulting Ophthalmic Surgeon, Guy's Hospital;

Hon. Fellow Downing College, Cambridge.

Born 1845. Died 1915.

WILLIAM ARTHUR BRAILEY, Ophthalmic Surgeon to Guy's Hospital from 1882 to 1905, died on April the 8th after a few days' illness in his 70th year. A strenuous worker all his life and devoted to his practice, he died, as he would have wished, in the midst of active professional work.

Born in 1845, the son of a Wesleyan minister, he was sent at the early age of 8 to the well-known Nonconformist school of Woodhouse Grove, where the Spartan system of hard work and hard living, in vogue at that time in such institutions, did much to inculcate that devotion to work and duty which lasted his lifetime. He remained at this school for six years, and the hardships and privations which the boys had to suffer, as some of his old school-fellows may remember, doubtless undermined his naturally delicate constitution. For the remainder of his life he was pursued by bad health, and only an iron will and vigorous mental activity could have accomplished what he did.

At the age of sixteen he matriculated at the London University, taking first-class honours, and in 1862, being then seventeen, he joined Guy's and entered the profession in which he

was to be so conspicuously successful, with no influence, and poorly equipped in health and means. At the entrance examination he took the first prize in Classics and Mathematics, no second prize being awarded. It is interesting to note that in the same prize list there are such well-known names as Thomas Stevenson, Henry Howse, George Savage, and Henry Morris.

After a year's work at Guy's, at the end of which time he was awarded an Exhibition, his health again broke down, so he went to Cambridge where his father was then living, and was elected to a minor Scholarship at Downing College.

At the University his career was an uninterrupted series of successes, and he won the esteem and friendship of such men as George Humphry and George Paget, then Professor of Anatomy.

In 1865 he was elected a foundation scholar of Downing, and gained prizes in 1865, 1866, and 1867. In 1867 he took the Natural Science Tripos, being placed second in the first class, in the days when candidates were placed in order of merit. In Anatomy and Physiology he gained the first place.

At the same time he was not less active at the London University, where he took honours in Classics, Anatomy, and Physiology, and in 1865 gained an Exhibition in Biology, and passed his B.A. with honours in Anatomy and Physiology in 1868. After taking the B.A. degree at Cambridge, he continued in residence for two years (1869—1871) as Intercollegiate Lecturer in Natural Science, and at the same time was one of the most successful private coaches.

In 1870 he qualified with the degree of M.B. Cambridge, and in the following year was elected a Fellow of his College.

Two years later he married Agnes Robertson, by whom he had two sons and one daughter, and went into general practice at Witham in Essex. In the following year, finding that his health was again breaking down, and being ambitious for something more than a general practice in a country town, he applied

for the Chair of Anatomy at Owen's College, and later, being advised to leave England on account of his health, he applied for the Professorship of Physiology at Otago, New Zealand. In spite of his candidature being backed by such men as Hilton Fagge, Cooper Foster, Habershon, George Humphry, Paget, and Pavy, he was unsuccessful in obtaining either post.

In 1874 he returned to Guy's and first began to devote himself to Ophthalmology, becoming attached to Moorfields, where he acted as Curator and Librarian from 1875 to 1881. At Guy's he was Lecturer in Comparative Anatomy and Zoology from 1878 to 1888, and held a similar post at St. George's Hospital at the same time. In 1882 he was appointed Assistant Ophthalmic Surgeon to Guy's, and remained on the Staff until his retirement in 1905.

It was while he was at Moorfields that he first met Sir William Bowman, and the two formed a firm friendship which lasted without interruption until the death of Bowman in 1892. In 1888 he was secretary to the Bowman Testimonial Fund which published the latter's collected papers. He was a prime mover in the formation of the Ophthalmological Society which came into actual being in 1880 with his friend Bowman as first President.

In the following year he was joint secretary with Nettleship of the Ophthalmological Section of the International Medical Congress, which then met in London, and he then formed life-long friendships with such men as Snellen, Donders, and Hansen Grut.

At this time he wrote many papers for the Ophthalmological Society's Transactions, Royal London Ophthalmic Hospital Reports, and in particular did much original work on Glaucoma and sympathetic diseases, subjects in which he seemed to take a special interest.

In 1885 he was Hunterian Professor at the Royal College of Surgeons.

On Bowman's death he succeeded to the bulk of his practice, and his very large amount of private work, together with his duties at Guy's, took up all his time, and he resigned the post of Ophthalmic Surgeon to the Evelina Hospital which he had held for some years.

His only daughter died in Burma in 1914, and he felt her death very deeply. He is survived by his wife, and two sons, both of whom have followed in his footsteps as Ophthalmic Surgeons.

With no inclination to publicity or desire for social amenities at any time, in the latter years of his life he seldom went out, and was only known to a few old friends. His brief holidays were spent simply and quietly at his Sussex farm, in the management of which he worked with unflagging energy.

Apart from his intellectual qualifications, his indomitable perseverance and will power would have raised him high in any profession.

SOME ACUTE ABDOMINAL PAINS WHICH DO NOT REQUIRE OPERATION.

By

Sir FREDERICK TAYLOR, Bart., M.D.

President of Royal College of Physicians, Consulting Physician to Guy's Hospital, Physician to the Seamen's Hospital, Greenwich.

We are indebted to the Editor of "The Universal Medical Record" for permission to reprint this article. It appeared originally in Vol. III., No. 1, of that Journal.

Acute pain in the abdomen has a real interest for both physician and surgeon, and our knowledge of its ætiology has very much increased of late years. One might almost with truth say that forty years ago the diagnosis of an acute abdominal pain lay between colic, peritonitis, and intestinal obstruction, so far as the alimentary canal and its appendages were concerned, while female patients had the additional opportunity of acute lesions in connection with the pelvic organs. We now know that colic and peritonitis must have included cases of appendicitis, cholecystitis, acute pancreatitis, the pains which may be felt over the front of the abdomen in a basal pneumonia, the gastric crises of tabes dorsalis, and others to which I may have to refer.

The treatment, too, in those days was as simple in one direction, that of drugs, as some would have it nowadays in the other direction, or that of surgery. Colic demanded purgatives, and peritonitis was treated with opium; and in view of the prevailing

belief in the principle of keeping the *primæ viæ* clear, it became the duty of teachers to warn the student of the danger of stirring up the intestines to vigorous action when they might already be inflamed on their serous surfaces, and when rupture at some or other point might conceivably follow. Even if obstruction by band, or internal hernia, was a possible diagnosis, it seemed wiser to ease the pain, and quiet the intestines with opium, than to hasten stercoraceous vomiting, and perhaps determine rupture, by the use of violent purgatives.

Surgery was reserved for cases in which a diagnosis of obstruction could be made with some certainty; for the very good reason that operations on the peritoneal surface were constantly fatal from the inevitable introduction of septic material within the peritoneal cavity. Operations for recognised strangulated hernia were systematically and dutifully performed, and they were no doubt more successful than operations upon the general peritoneal cavity, now called laparotomy; but the frequency with which these cases died within twenty-four or forty-eight hours of the operation, in spite of the absence of classical signs of peritonitis, was sufficiently appalling. And in medical cases, that is, cases of peritonitis not due to external hernia, there is no doubt that the treatment by opium was often successful, so long as the drug was given fearlessly in full doses frequently repeated. In this way patients, entirely unused to the drug, have taken from six to twenty grains of opium in the day, for six or more days consecutively, and have recovered from most threatening symptoms. What was the nature of these cases, we cannot, of course, with confidence say; but that some were peritonitis started by appendicitis there can be no doubt. That surgery could be of any use in such cases, that the source of the peritonitis could be got at, and removed successfully, or that the knife could do anything but relieve mechanically a bowel blocked by band or kink, seemed in the days before Lister scarcely to have been conceived. Even with regard to obstruction itself, the dangers of surgery were so strongly felt that a distinguished surgeon

advocated in such cases the processes of inversion of the patient and kneading of the abdomen before a cutting operation was brought into requisition.

The position now is very different. The comparative immunity from danger which laparotomy, in connection with aseptic methods, now possesses justifies operation in a very large proportion of cases, not only as a curative measure, but as an aid to certainty in diagnosis. At least twenty years ago I heard the opinion expressed by an able surgeon in the north of England that the impossibility of an accurate diagnosis in acute abdominal pain rendered an operation always justifiable. Whether he would have sustained that without qualification in a reasoned thesis may be open to doubt; but it expressed at any rate a strong feeling as to the difficulties of diagnosis and the safety of operation.

But the range of knowledge has extended considerably since that time, and while it must be admitted that the close similarities among some cases of acute abdominal pain is such as to need the help of the surgeon in order to *see* what is going on behind the anterior abdominal walls, it is very evident that there are other cases in which the resources of clinical medicine are sufficient to guide one as to the nature of the case, and to make any assistance from the knife quite unnecessary.

One class of cases is that in which the onset of a dorsal pneumonia or pleuro-pneumonia is accompanied by severe abdominal pain. This has been long known to physicians; but when an operation was being regarded as the chief means at arriving at a diagnosis, or the only method of cure, it was desirable that this relation between the chest and the abdomen should be more widely recognised. The late Mr. Harold Barnard brought some cases of the kind before the Clinical Society in 1902, and his introductory remarks are as follows.* "Thoracic diseases in some cases produce the most deceptive abdominal signs. Modern

*Clin. Soc. Transactions, Vol. xxxv., 1902, page 122.

standard works of medicine contain only a meagre reference to this condition, and it is apparently unknown to surgeons, if we may judge from their text-books." But he points out later that Andral, Watson, and Fagge had recognised that peritonitis or hepatitis might be simulated by pleuro-pneumonia. The simulation was very close indeed in a case of mine years ago, in which an elderly woman had acute pain and tenderness over the liver and right flank together with jaundice. The physical signs of an acute right basal pneumonia were soon manifest, and as the pulmonary signs cleared up, the jaundice also promptly disappeared. The jaundice, which though known as an accompaniment of pneumonia, is relatively rare in that connection, no doubt contributed to render a correct diagnosis difficult. Within a fortnight a similar case, but without jaundice, occurred in an adjacent medical ward.

The onset of pneumothorax has also been accompanied by violent abdominal symptoms deceptively like those of perforative peritonitis.

Perhaps one of the most important groups of cases in which severe abdominal pains may be misunderstood and lead to a laparotomy is that formed by the gastric crises of locomotor ataxy or tabes dorsalis. Without inquiring too closely how often this has been done, it is sufficient to say that it has been done more than once. I was told of one case in which a patient was sent to hospital for frequently recurring attacks of abdominal pains; an operation was performed, and he was sent home. The pain recurred, the wound was re-opened, the parts investigated, and the wound closed. The pains recurred, and either then, or after another fruitless operation, a physician was asked to see the case, and discovered that he had tabes dorsalis.

I have seen lying in three beds at the same time, patients with early locomotor ataxy all of whom had been operated upon. Two of them, it is true, had local signs suggestive of changes which might have been relieved by operation, but the changes found were very inadequate as explanations of the vomiting, and

as a fact the pain and vomiting persisted after recovery from the laparotomy. In the third case the patient had suffered for more than four years from pain and vomiting; he was correctly informed at a hospital in London as to the nature of his case, but shortly afterwards at an infirmary in the country his case was diagnosed as pyloric obstruction and a gastro-enterostomy was performed. After this, as a fact, but I will not suggest as a consequence, the gastric attacks were more frequent and of longer duration on each occasion.*

A third disease in which abdominal pain may be severe enough to invite surgical interference is diabetes. That diabetic coma is often ushered in by severe epigastric pain has long been known. I remember many years ago, that when in the wards of the hospital, I was told casually by the house physician of one of my colleagues, that he had a patient under his care who had been seized with such intense pain that he thought he must have a perforated gastric ulcer. He said he was under treatment for diabetes. I at once warned him that the patient might be passing into diabetic coma, and this proved to be the case.

But I think it is only comparatively recently that this form of pain has also nearly come within the sweep of the surgeon's knife. Particulars of cases of the kind will be found in the pages of the "Lancet."†

* Soon after writing this I became aware that operations had been undertaken for the relief of gastric crises, but not operations of the kind contemplated in this paper. The obviously nervous origin of the abdominal symptoms has led surgeons in France and Germany (Foerster, Francke, Lambret, and others) to try and prevent the attacks by resection of the dorsal spinal nerve-roots, by stretching or resecting the intercostal nerves, and even by bilateral section of the vagi at the cardiac end of the stomach. The results are not brilliant. Some patients are said to have been cured; in others after temporary cessation the attacks have recurred; many patients have died. Only very severe attacks, frequently repeated, and of many years' standing, would justify these operations.

† *Lancet*, 1909, Vol. ii., page 1609; *ibid.*, page 1773; *ibid.*, page 1987. 1912, Vol. i., page 378; *ibid.*, page 647.

The first of these notices is based on two cases reported in the "Inter-Colonial Medical Journal of Australia." A boy, aged fourteen, had pain and vomiting, and was regarded as suffering from intestinal perforation. The abdomen was prepared for laparotomy, and the surgeon was about to operate when it was found that the urine contained sugar and gave the ferric-chloride reaction. At that time he was semi-conscious, and later he became more comatose and died. The other patient was a child, aged eight, under treatment for glycosuria; vomiting and paroxysmal abdominal pain occurred ; acute intestinal obstruction was diagnosed, and two medical men agreed in the necessity for operation. Some change in the abdominal symptoms, and the appearance of coma, led to the operation being abandoned, and an alkaline treatment by vein and mouth was followed by recovery. Another of these cases is recorded as having simulated appendicitis.

In the obscure disease known as Henoch's purpura severe abdominal pain is a characteristic feature ; and an interesting point in the present connection is that the abdominal symptoms may occur early in the case, while the purpura, from which the disease is named, is later, and may be relatively slight in extent. Dr. Sutherland, in an interesting paper entitled "Gastro-Intestinal Crises from Effusion into the Bowel Wall,"* has collected a number of these cases: in which it is clear that the pain was due to hæmorrhage into the wall of the intestine. In not a few a laparotomy was performed. Sometimes, it is true, a mass was felt in the abdomen, and the close resemblance to intussusception was especially noted by Dr. Sutherland. But the hæmorrhage into the wall of the bowel may itself be the cause of an intussusception of the damaged part of the gut, so that a diagnosis is often difficult and complicated. However, it appears to be clear that in the absence of a tumour, and unless the evidence of intussusception is very strong, it is undesirable

*Proc. Roy. Soc. of Med., Med. Sec., Vol. ii., page 265.

to operate, as further hæmorrhage and sloughing are likely to follow, and apart from intussusception, the operation can do no good.

Some two years previous to the reading of Dr. Sutherland's paper, I had some experience of the condition in a schoolboy, aged ten, who began to be ill with mild pyrexia. About the fifth day of his illness he vomited, and had some diarrhœa; and two days later he was collapsed with feeble pulse, and then had an eruption of purpuric spots on the elbows, knees, arms, ears, and cheeks, but few, if any, on the trunk. On the ninth or tenth day the diarrhœa had been checked by morphia, but he now had a quick pulse, was lying on his back with knees drawn up, deep thoracic breathing, scarcely any movement of the abdomen, which was tense, but not full, much tenderness in the right iliac fossa, as well as in the left iliac fossa, and over the body generally. No dulness over the cæcal region or in the abdomen generally. Sometimes he was throwing himself about. He vomited twice the following night, but the next day the abdomen, though moving little, was more supple; and the resemblance to peritonitis gradually grew less, though he had abdominal pains, which were relieved by morphia, for some days afterwards. Some of the petechial spots sloughed, and albumen appeared in the urine, with casts—the evidence of a nephritis which persisted for months.

Allied to the above are the rare cases of mesenteric embolism and thrombosis, in which acute abdominal pain and vomiting occur, and may be rapidly followed by death. In a case I reported* death took place within eighteen hours of the onset of pain. In these cases there is free hæmorrhage into the intestinal wall, and operation seems out of court.

In the above cases we see that from the point of view of causation, they fall into three groups: those which are due to referred pains or functional nerve failure; one in which toxæmia

*Pathological Transactions, 1881, vol. xxxii., page 61.

appears to be the cause; and two in which actual lesions in the abdomen set up an obviously local pain. Another case belonging to the first group, to which I need make but little reference, is the neurotic or hysterical simulation of gastric ulcer by pain and vomiting, not so much as a solitary occurrence, but as a repeated event; and this has not infrequently led to an operation. This pain is often accompanied by vomiting, with the appearance of blood in the vomited matter; and the repetition of the symptoms after repeated improvement has in some cases justified the close investigation, by means of operation, of the actual condition of the abdominal organs.

As a companion to the occurrence of epigastric pain in diabetic coma, and as an illustration of an abdominal pain due, not apparently, to local lesion, but to toxic influence, may be mentioned the fact that severe pain in the epigastrium, described as "epigastralgia," has been seen as the result of the injection of microbic serums for the treatment of disease. These cases were referred to in the *Lancet*,* and were taken from the "Progrès Médical" of March 16th and May 11th. In the first case 230 c.c. of antitoxic serum were injected over a period of nine days for the treatment of diphtheria; and at the end of this time the patient had nausea, vomiting, a raised temperature, extensive urticaria, pains in most of the joints and in the muscles, so that he could not turn in bed. On the eleventh day after admission—the third after cessation of the injections—epigastric pain began and was accompanied by vomiting and diarrhœa. The pain was severe, situate deep in the epigastrium, continuous, but subject to violent exacerbations, causing the patient to sit up in bed with the thorax acutely flexed on the abdomen. Temporary relief was obtained from morphia, and the pain gradually subsided. In the second case 20 c.c. of antimeningococcic serum were injected into the spinal canal for the treatment of meningitis in a man aged thirty-eight. Almost immediately there was epigastric pain so severe that the man kept his legs flexed on the abdomen in

* *Lancet*, 1912, vol. i., page 1422.

order to relieve it. Delirium and convulsions followed, and he died ten hours after the injection. Death was attributed to the injection, and no abdominal lesion is reported which could have accounted for the pain.

These, of course, are cases which, from the circumstances attending the pain, would not be likely to invite the operation of laparotomy, but they are interesting as showing how many other sources of pain there are besides an acute local lesion.

I may also very briefly refer to the cases of abdominal pain, an instance of which Sir Lauder Brunton brought before the Royal Society of Medicine in March* last under the name "Angina Abdominis." The pain was brought on by exertion, was most severe in the umbilical region, to which it was at first confined; but it gradually increased in severity and spread all over the front and back of the chest. The pain was regarded as probably due to spasm of abdominal vessels, and as being related to ordinary angina pectoris; it was relieved by the use of trinitrin. Other similar and allied cases have been reported abroad; but, on the whole, it does not seem that such cases would be regarded as coming within the province of surgery.

I have not, of course, exhausted the list of painful abdominal affections which do not call immediately for operation; there remain, for instance, the different forms of colic—intestinal, renal, and hepatic—but these have long been familiar, and do not need further comment.

It remains to ask if there are any special means the surgeon or physician can take to avoid the possibility of an error, so that an operation may not be undertaken unless absolutely necessary, either for treatment or to clear up a diagnosis otherwise insoluble. As in so many other cases, the surest help to a correct diagnosis is the recognition, and the recollection at the given moment, that the disease or condition which is present may actually give

*Proc. Roy. Soc. of Med., Med. Sec., vol. v., 1912, page 54.

rise to the symptoms of pain. To remember that in basal pneumonia, tabes dorsalis, and diabetic coma, acute epigastric or abdominal pain may occur, is half the battle. The tests for the underlying conditions may then be applied; for instance, in pneumonia the examination of the chest, and the counting of the rapid respirations; in tabes dorsalis, the examination of the pupils and the knee-jerks, and inquiry into the history of lightning pains and of previous abdominal attacks; and in diabetes, the tests for sugar in the urine.

The local symptoms are few, and, as we have shown, the possible causes are many. Pain, the chief of these symptoms, that which compels us to take action, is deceptive in its varying distribution. It must, indeed, be admitted that the attempt to distinguish the various sources of pain by the characters of pain, by its localisation, and by such other abdominal symptoms as vomiting, distension, rigidity, etc., has not been eminently successful; and its failure has been the chief reason, perhaps, for the prompt recourse to operation. One may instance the occurrence of pain on the left side of the abdomen in cases of acute appendicitis, and the simulation by chronic appendicitis of gastric and duodenal complaints as illustrating the difficulties.

Failing distinctive features in the pain, we turn to vomiting and to the condition of the abdomen. Vomiting is not so constant as pain; it occurs especially at the commencement of an attack whatever the cause of the pain, and it may be repeated from time to time, especially if food be taken; but it may soon become infrequent if food is withheld. The state of the abdomen is also variable; often in the first few hours after a perforation the abdomen is not distended, but flat, rigid, with hard recti, and respiratory movements entirely absent or very slight. If there is much gas extravasated from the ruptured viscus, the abdomen may be distended, and the hepatic dulness may be lost. If the stomach is empty, or the duodenum or jejunum is the ruptured organ, no distension may occur until inflammatory changes have led to paralysis of the intestinal coat.

It is interesting to ask whether in the gastric crises of locomotor ataxy there is anything sufficiently constant or sufficiently distinctive to help one to a certain diagnosis even apart from the absent knee-jerks and Argyll-Robertson pupil; or rather to suggest to the surgeon or practitioner hitherto unacquainted with the patient that these points should be investigated.

Inquiry into the details of gastric crises will show that incessant vomiting is a characteristic feature, vomiting which may go on for several days accompanied generally by epigastric or abdominal pain; but not generally by much tenderness, rigidity, or distension of the abdomen. And the attack subsides, sometimes suddenly, and recurs after some months. The vomited matter is often abundant, and after food has been got rid of, consists of quantities of thin fluid—dirty water, as it is sometimes described tinged with green. The abdomen may be retracted, or at least not distended; and the patient often writhes about, or doubles himself up, in the effort to get relief.

These features, if not distinctive, and not absolutely constant —for pain occurs sometimes without vomiting—are different from those which are most characteristic of perforation and acute appendicitis, the lesions which most often require immediate operation. In many cases, of course, the history of numerous previous attacks, at intervals of weeks or months, would put one on guard. But it may fairly be urged that in a first attack in a given patient such a history cannot be forthcoming. At least, in some cases, the first attacks are not of such severity, or of such long duration, as those which occur later; but even an early attack might be sufficiently severe to mislead, and both in such a case and in others where repeated attacks are believed to indicate a persistent lesion, such as chronic appendicitis or pyloric stenosis, or other organic change, the protection must lie with the clinical tests of the knee-jerk and Argyll-Robertson pupil, and with the history of lightning pains.

In diabetes the fact of glycosuria is often well known long before any nervous symptoms appear, but this is not always the

case. Often, however, the patient has already become somewhat drowsy, that is, the toxæmia is already affecting the brain before the epigastric pain is felt; and it is especially noted in the two cases quoted by the *Lancet* from the "Progrès Médical"* that the characteristic dyspnœa of diabetic coma was already commencing. It seems to me regrettable that Jaccoud should have described such cases as a "peritonitic form" of diabetic coma, seeing that peritonitis is not found in these cases; and surely things should be named after what they are, and not after what they seem to be, but are not.

With regard to distinguishing features in the abdominal symptoms of Henoch's purpura, Dr. Sutherland lays stress upon the patients throwing themselves about in consequence of the pain, an event which he says does not happen in cases of peritonitis.

**Lancet,* 1912, vol. i., page 378.

PARTIAL GASTRECTOMY FOR CARCINOMA OF THE STOMACH.

By

R. P. ROWLANDS, M.S.

Total gastrectomy is very rarely necessary, for when malignant disease is so extensive as to invade the whole stomach, it is usually incurable for other reasons, such as extensive adhesions or secondary growths. The technical difficulties are so great as compared with those of sub-total gastrectomy, that it is desirable whenever possible to save even a small healthy portion of the cardia. This makes the anastomosis very much easier. The chief indication for the operation is that variety of chronic diffuse carcinoma of the stomach which produces a small leather-bottle stomach, the "linitis plastica" of Brinton. Fortunately secondary growths (and extensive glandular infection) are rarely associated with this condition.

It is more than probable that the internal secretion of the gastric mucosa is necessary to life, for the subjects of complete gastrectomy gradually become anæmic and marasmic. This makes it important to save a little of the cardiac end.* Therefore, partial gastrectomy is practically the only operation for malignant disease of the stomach.

In this operation a large but variable part of the stomach is removed; an inch of the duodenum and the greater part of the

* Lancet, 1911, vol. ii., p. 430.

stomach are resected, so that the channel can be re-established only by gastro-jejunostomy engaging the cardiac remainder. With a great reduction in its mortality this operation is more and more frequently performed both for malignant and innocent ulcerations. For carcinoma, although it may not always eradicate the disease, it offers both a greater prolongation of life and greater relief than gastro-jejunostomy, without seriously increasing the immediate risk. It is often difficult to be sure that a chronic ulcer is innocent, even with the aid of immediate microscopic examination, and for this reason resection should be performed in doubtful cases, whenever practicable, without greatly adding to the risk. Moreover, a callous simple ulcer may become malignant in spite of gastro-jejunostomy. Malignant disease is nearly always carcinomatous, but sarcoma is not so uncommon as it is generally supposed to be.* The writer has performed partial gastrectomy in one case.

It is significant and fortunate that in the large majority carcinoma, like simple ulcer of the stomach, starts at or near the pylorus upon the lesser curvature. Significant, because of the undoubted risk of a chronic ulcer becoming malignant; fortunate because a growth in this situation—

(a) Soon leads to obstructive signs of great value in diagnosis;
(b) The growth is often palpable in the epigastrium; and
(c) Is favourably placed for resection if the diagnosis is made in time.

In a few cases carcinoma commences at the cardia or in the fundus, where radical operation is rarely practicable. Growths upon the anterior or posterior walls near the middle of the stomach are more amenable if they are discovered in time, but this is unusual, for they do not cause obstruction or early symptoms. Without operation cancer of the stomach is absolutely

* Gosset has collected 171 cases, with 13 gastrectomies and 10 deaths. Metastases are much less common than with carcinoma (Ann. of Surg., 1911, vol. ii., p. 313).

hopeless. Spontaneous cure is not known, and medicine is of no use except to alleviate the symptoms of inoperable disease. Surely surgery can do better than this if given a chance, but too often the surgeon is not asked to see the patient until the diagnosis has become too obvious and the prognosis is hopeless.

Diagnosis.—Much time is wasted on laborious attempts to arrive at a diagnosis from various laboratory tests. This "scientific and deadly delay" (Mayo) often throws away the opportunity of radical and successful operation. The laboratory tests must be regarded as nothing more than aids in the diagnosis. For instance, free HCl, although usually diminished, may be found even in excess with early gastric carcinoma. It may be greatly reduced in pernicious anæmia, chronic pancreatitis, or hour-glass stomach. Blood corpuscles may be absent. Apart from obstruction, X-ray examinations are not of great value in early cases. Gastroscopy is not yet reliable in excluding carcinoma, and the same is true of examinations of blood serum. Cancer of the stomach in its early stages does not give rise to symptoms which can be said to be characteristic of the disease. Rapid and progressive wasting, anæmia, pain, anorexia, nausea, and vomiting are suggestive. These, and especially a palpable tumour or obstructive signs, however, indicate an early exploration. Some half-cooked rice and a few raisins are given with some soup in the evening. If on washing out the stomach in the morning any food remnants are found there is clearly obstruction, and although this may be due to a simple ulcer, it strongly indicates an operation both for diagnosis and treatment. *It cannot be too strongly urged that diagnosis to be early enough must frequently be made by exploration.* Operation is delayed because the *immediate mortality* is generally supposed to be very high, and the *prospect of permanent cure or prolonged relief is believed to be poor.*

As regards the *immediate mortality,* the technique of partial gastrectomy has been so much improved in recent years that in the last hundred cases operated upon at St. Mary's Hospital

(Rochester) there was a mortality of 7 per cent.; in the last fifty 4 per cent.*

It is imperative to remark here that resection for definite malignant disease is not likely to be attended by such brilliant results unless the patients come for operation much earlier than they do in this country at the present time. When the growth and infected glands are freely movable, resection is not a very formidable and dangerous operation in good hands, but in later cases the operation may be very difficult and dangerous. A careful selection of cases suitable for resection is imperative.

As regards *ultimate results*, out of ninety patients who have been traced for over three years after operation, 36·6 per cent. are alive; out of fifty-eight traced over five years after operation, thirteen, or 22 per cent., are known to be alive and well. "These data would indicate that the patient with cancer of the stomach, which is sufficiently localised to be removed radically, has better than a 90 per cent. chance to recover from the operation, and better that a 36 per cent. chance of a three years' cure, and at least a 25 per cent. chance of a five years' cure." (Mayo, *loc. cit.*)

Indication for Resection.—As it is, less than a third of the cases of carcinoma of the stomach are diagnosed early enough to allow a radical operation.

(A) *Without exploration, how are we to tell if a case is inoperable?* This is not possible in many cases, as shown by the following table :—

Cases of Cancer of the Stomach examined in the Mayo Clinic between January 1st, 1908, and September, 1909.

Total number	335
Hopeless and not admitted	146
Resection	78
Gastro-jejunostomy...	39
Excision of malignant ulcer	2
Exploration. Inoperable disease found	70

* Mayo, Surg. Gyn. and Obst., February, 1912.

The following *clinical signs* indicate that the growth is inoperable, and that it is inadvisable to submit the patient to an exploration :—

(i.) The discovery of dropped and grafted nodules of growth in the pelvis on rectal or vaginal examination.

(ii.) Enlarged supra-clavicular glands, especially common on the left side.

(iii.) Nodules of growth at the umbilicus or under the skin of the abdomen.

(iv.) Ascites, indicating peritoneal growth or obstruction of the portal vein.

(v.) Nodular enlargement of the liver.

(vi.) Moreover, the patient may be too exhausted to stand the operation.

(B) *Upon exploration* the following points indicate that the growth is unsuitable for resection :—

(i.) *Secondary Growths in the Viscera,* especially in the liver. The hand is always passed above as well as below both lobes of the liver, for it is not uncommon to find isolated nodules of growth upon the diaphragmatic surface of the liver. A direct local invasion of the anterior edge of the liver is not always a contra-indication, for a wedge-shaped piece may be resected with the primary growth. More often an invaded gall-bladder, or even a part of the transverse colon, may be removed. Invasion of the pancreas has been usually regarded as a strong contra-indication, but recent work has shown that portions of the pancreas may be safely removed.

(ii.) *Peritoneal Infection.*—The hand is passed into the pelvis and the small intestine is inspected. If nodules of growth are discovered, it is generally useless to attempt resection of the primary growth, but an isolated nodule in the pelvis need not necessarily interfere, for it may be either removable or of slow growth, so that prolonged *relief* may be expected from resection.

(iii.) *The Size, Site, and Degree of Fixation of the Growth.*—While in many cases cancer of the pylorus may remain long limited to the pylorus itself, it is very liable to infect the omenta and the lymphatic glands around the head of the pancreas, and later to cause secondary growths in the liver and other parts.*

Adhesions, too, are very frequently met with between the stomach and the colon, pancreas, or liver. When adhesions are present, the immediate mortality of the operation is greatly increased, and this is especially true of adhesions involving the pancreas. The prospects of permanent relief are, of course, much diminished, for the growth follows closely in the wake of inflammatory adhesions. *The more the growth has extended towards the cardiac orifice along the lesser curvature, the less the chance of successful resection.*

Moderate enlargement of the lymphatic glands is not a contra-indication to resection, for the glands are very frequently found to be merely inflamed, and they may be seen near a simple ulcer. When the glands are of large size and adherent or widespread, it is generally too late to attempt the removal of the growth. In the great majority of cases an exploration should be undertaken before any tumour can be felt, but it is certainly not true that resection is to be considered impracticable because a tumour is evident, for even the induration around a simple pyloric ulcer may be felt in thin patients. It must not be concluded from the apparent mobility of a growth felt through the abdominal wall that a resection is practicable, or vice versa.

From a careful consideration of the symptoms, and the results of chemical and microscopical examinations of the gastric findings, etc., the diagnosis should be more frequently made before the growth becomes irremovable; and with this object an early exploration should be undertaken, when the symptoms do not yield to treatment and suggest the probability of the existence

* McArdle (Dublin Journ. Med. Sci., vol. lxxxiii., p. 511), having collected from the statistics of different writers 1,342 cases, states that the pylorus alone was involved in 802, or over half the cases.

of carcinoma of the stomach. The danger of an *early* exploration is very small, although a simple exploration in *late and inoperable* cases carries with it a considerable risk, as shown by the experience of Kronlein and Mikulicz, who had a mortality of about 9 per cent. in such late explorations.

The researches of Cuneo, MacCarty, Boorman, and others have taught us much about the ways in which carcinoma of the stomach spreads. This information is of great value in telling us when and how to attempt resection. It is fortunate that—

(a) *Dissemination into the Liver and other Viscera* is a late event.

(b) *Lymphatic Infection.*—A great deal depends upon the lymphatic drainage of the stomach and of the cancer-bearing area, which in 80 per cent. of the cases is to the right of a line continued downwards from the right border of the œsophagus. The lymphatics drain into the glands in the gastro-hepatic and gastro-colic omenta. The glands in the lesser omentum are fairly numerous, and consist chiefly of two groups, one about the coronary artery, and another just above the pylorus. Those in the gastro-colic ligament are all to the right of the line already mentioned, and they are especially numerous just below the pylorus. The lymphatic current is chiefly towards the right, and soon carries the infection to the group of glands lying near the head of the pancreas to the right of the cœliac axis. There is very little tendency for the disease to spread along the greater curvature towards the left into the fundus, which can be safely left in pyloric and prepyloric growths which form the large majority of gastric cancers. Along the lesser curvature there is a great tendency for the disease to spread to the left both in the stomach-wall and in the lymphatics. In some cases the primary lymphatic glands escape, while the secondary ones are invaded. Occasionally there is an erratic spread so that the glands in the transverse meso-colon may be invaded early. Infected glands vary much in size, and without microscopic examination it is impossible to be sure whether a gland is or is not invaded. The

only safe way is to remove all the draining lymphatic glands. In view of the occasional infection of the great omentum it is also wise to remove it as well as the lesser omentum. The degree of lymphatic infection varies very much, and does not seem to have any very distinct relation to the position or size of the primary growth. Both the immediate risk and the ultimate prognosis depend very much upon the degree of lymphatic infection.

(c) *Local Spread.*—The disease spreads by permeation of the lymphatics of the stomach, especially those in the submucosa, and especially along the lesser curvature towards the cardiac orifice. The growth often seems to end abruptly at the pylorus, but microscopic examination has shown that permeation extends a little beyond this into the duodenum, so that it is always wise to remove at least an inch of the duodenum.

(d) *Peritoneal Infection.*—Nodules of growth are commonly found in the peritoneum, especially at the bottom of the pelvis, and later upon the peritoneal covering of the small intestines. This is due to the direct infection by cancer-cells which have escaped into the peritoneal cavity and gravitated towards the pelvis.

Therefore, it is clear that resection to be ultimately successful must be wider than hitherto, both as regards the stomach and the lymphatic vessels and glands. The immediate mortality does not seem to have increased with the amount of stomach resected, nor is the mortality of a well-planned resection in late cases much greater than that of gastro-jejunostomy, whereas the amount of relief and extension of life obtained is very much greater in resection. Usually the average relief after gastro-jejunostomy for growth is only about four months, and this relief is often incomplete owing to the presence of the ulcerating and decomposing growth.

The more frequent excision of callous gastric ulcers will do much to prevent the development of cancer of the stomach, and many a developed but unsuspected cancer will be removed at an early and hopeful stage. The ideal is to operate at an early

stage before the growth has become adherent to vital parts and before the lymphatic glands have become invaded. Both the immediate and ultimate results of the operation will rapidly improve as this ideal is approached.

Operation.—It is very important to prepare these patients thoroughly for at least three days before the operation. A free incision is made near the middle line extending from the epigastric angle downwards a little below the umbilicus. A thorough exploration is rapidly carried out to determine if an attempt at resection should be undertaken. If resection be decided upon, axillary infusion is commenced and carried out throughout the operation. The large vessels are at once ligatured to limit hæmorrhage and shock (see Fig. 1). This step also makes the operation much easier and saves valuable time. The lesser omentum is opened in a bloodless part close to the liver, and the pyloric artery is divided between two ligatures, tied well above the pylorus and the group of lymphatic glands in this situation. The common-bile duct and hepatic artery are carefully avoided, as they lie on the portal vein in front of the foramen of Winslow. Adhesions between the liver and the growth may have to be separated to allow this step to be carried out. The upper border of the pylorus and duodenum are cleared for two inches, and any vessels that bleed are at once tied. The stomach is drawn downwards and to the right, while the gastric artery is carefully tied and divided near the cardiac orifice, and the lesser omentum is separated from the lesser curvature for about an inch and a half. The lower border of the stomach is then examined, and the left gastro-epiploic is divided between two ligatures at the selected point, which is well to the left of the lymphatic glands in the gastro-colic omentum, and also to the left of a line continued downwards from the right border of the œsophagus. The lower border of the stomach is cleared for about two inches. The great omentum is then carefully separated from the transverse colon, and any bleeding points are at

be more difficult when inflammatory adhesions exist around a large growth. Several ligatures are generally required at the upper and left attachment of the omentum. The stomach and omentum are then separated from the transverse colon and meso-colon, great care being taken to avoid injury of the meso-colic vessels. The bloodless area of the transverse meso-colon, if adherent to the stomach, should be removed with it, and the opening thus made may be used for the gastro-jejunostomy later on. The meso-colic artery is carefully traced to its origin below the pancreas, and any glands upon it are removed by gauze dissection. Injury or obliteration of this artery may cause gangrene of the transverse colon, although the anastomosis between its branches and the right and left colic arteries usually preserve the circulation of the bowel. Such an injury can usually be avoided by care and gauze dissection. The great omentum and pyloric pouch are drawn up and the glands lying below the pylorus are very carefully separated from the pancreas, and the right gastro-epiploic artery is tied and divided near its origin. Sometimes the gastro-duodenal has to be tied when the lymphatic glands are large and adhesions numerous. Great care is required in separating the pylorus, the first part of the duodenum, and the pancreas, and in some cases this step has to be deferred until a later stage of the operation after the duodenum has been divided, when a better view can be obtained, and some of the adherent pancreatic tissue can be shaved off and removed with the growth. The raw surface thus left is covered by suturing the posterior peritoneum over it. The lower border of the duodenum is cleared for about two inches. The primary growth, the chief draining lymphatic glands, and the omenta have been isolated in one mass, and the important vessels have been tied. Packs are now carefully placed behind and around the stomach. The duodenum is divided between two clamps one inch to the right of the pylorus and the cut edges are cauterised (see Fig. 2). The pyloric end of the stomach is drawn out of the way, turned over to the left, and protected while the duodenal stump is closed with a continuous catgut suture starting at the

upper border and passed around the blades of the clamp until the lower border is reached, when the clamp is removed, the suture drawn tight, and its ends tied together. The suture controls all bleeding and puckers the stump. Two purse-string sutures of linen thread are then used to invaginate the stump (see Fig. 3). The final one picks up some of the pancreatic sheath, and thus serves to turn the end of the stump backwards and bury it in the pancreatic tissue. Some of the posterior parietal peritoneum may also be brought over the end. All bleeding from the region of the pancreas is carefully stopped. An opening is now made in the large bloodless area of the transverse meso-colon, and the first loop of the jejunum is brought up and is sewn by a sero-muscular suture of strong black thread to the back wall of the stomach along an oblique line three-quarters of an inch to the left of and parallel to the line selected for the section of the stomach. To enable this to be done easily, the stomach is drawn well downwards to the right and then forwards by an assistant. The diseased part of the stomach is thus used as an excellent tractor and makes a step, otherwise very difficult, comparatively easy. Care is taken to avoid tension upon the jejunum. The part used for the anastomosis generally begins about four or five inches from the origin of the jejunum, and this point engages the stomach close to the œsophagus, and the suture line runs obliquely downwards and to the left so that the food on leaving the stomach easily gravitates into the distal part of the jejunum (Fig. 4). When this suture has been completed, the stomach is divided between two clamps, along the selected line. An opening the same size as the cut section of the stomach is now made in the jejunum, and the anastomosis is completed as in gastro-jejunostomy, strong catgut being used for the continuous deep suture. During this part of the operation the attachment of the cardiac end of the stomach to the jejunum prevents undue retraction and greatly facilitates the insertion of the deep suture. Then the sero-muscular suture is completed in front, and the opening in the transverse meso-colon is closed around the jejunum. Any of the

great omentum remaining to the left of the section in the stomach is brought up and sewn in front of the anastomosis. This method is far simpler and better than the old method which is shown in Fig. 5. It saves much time and is less likely to be followed by necrosis with temporary gastric fistula.

End-to-end union is rarely suitable when the resection is made for growth, for in spite of mobilisation of the duodenum after Kocher's method, there would be too much tension upon the suture line. In some cases of pylorectomy for callous simple ulcer, the open end of the duodenum may be joined to the posterior surface, but not to the much larger cut surface of the stomach. The disparity in the size of the two openings nearly always leads to imperfect suturing and leakage at the "dangerous angle." It is quite a different thing to make an end-to-end union after resection of early malignant growth or a callous ulcer occupying the middle of the stomach. Then two ends of similar size can be joined well and safely together. Some surgeons advocate the performance of gastro-jejunostomy immediately before the resection, and if the patient is not doing well at the end of the gastro-jejunostomy, the resection can be deferred until another day. Moreover, a doubtful growth can be microscopically examined during the gastro-jejunostomy. I do not like this method, because a preliminary gastro-jejunostomy may interfere with a proper resection, and the retraction of the cardiac portion of the stomach which follows the resection may drag upon and kink the jejunum. Deaths have occurred from this cause. It is better to first perform a wide resection and then to make the gastro-jejunostomy suitable to the occasion. The primary examination of doubtful tumours is not as yet thoroughly reliable. Moreover, a large callous ulcer closely simulating growth is better resected. As regards a two-stage operation, the combined risk of the two operations is greater than that of immediate resection, and, further, the patient, if he recovers after gastro-jejunostomy, is often so pleased with his condition that he fails to see the advantages of another operation until it is too late.

ILLUSTRATIVE CASES.

CASE 1.—J. W., æt. 51. Patient of Dr. French. Recovery. Recurrence four and a half years later. Gastric symptoms for four months. Vomiting anorexia, indigestion, constipation, chronic hæmatemesis and melæna, very severe anæmia and wasting; lost 22 lbs. in fifteen days.

Operation, November, 1909.—Large ulcer obstructing pylorus. The writer performed extensive, but not complete, gastrectomy; draining glands and omenta removed; duodenum closed; gastro-jejunostomy. Microscopical section shows carcinoma. Operation lasted fifty minutes.

Patient, three and a half years after operation, quite well and doing his ordinary work as a lift conductor. He had gained over three stone in weight. At first he could only take small meals; very small remainder of stomach had considerably dilated, as shown by X-rays. He died of recurrence in the pancreas and liver $4\frac{1}{2}$ years after the operation.

CASE 2.—Man, æt. 47. Patient of Dr. Carpmael. Recovery. Well three years later. Patient had indigestion and rapid wasting for about two months. He was watched in hospital for about a week, and it became clear that he ought to be explored, although an X-ray examination did not show any pyloric obstruction. It was thought probable that he had either a duodenal ulcer, or a growth of the pylorus. No swelling could be felt, but there was a great deal of pain and some tenderness to the right of the middle line in the epigastrium.

Operation on December 2nd, 1912.—Dr. Shipway gave ether by the intra-tracheal method. Abdomen was opened through inner and upper part of right rectus. A pyloric growth was at once found. It was nodular and white on the surface, having clearly invaded the peritoneal surface. No growth could be found in the liver or in the peritoneum. Special care was taken to examine pelvic peritoneum, which was healthy. There were two very large glands lying behind and below the growth in front of the head of the pancreas. They were movable. It was therefore decided to resect. Gastric artery was tied close to œsophagus, and the left gastro-epiploic artery was tied just beyond the left margin of great omentum. Great omentum was detached from transverse colon with ease. Several bleeding points were tied. As the right border was approached, the detachment became more difficult, and a perforation was made in the bloodless part of transverse meso-colon. This perforation was later useful for the gastro-enterostomy. Stomach was then clamped and divided in a line extending one inch to the right of œsophagus downwards and to the left. Cardiac pouch was closed with four layers of silk. Pyloric end was protected with gauze and gradually liberated, the whole of greater omentum and most of lesser omentum being removed, together with enlarged glands already mentioned, and one or two more in lesser and greater omenta. Gastro-duodenal vein and artery were tied separately, also a branch of

the hepatic. The duodenum was divided one inch away from pylorus, which was sewn up and invaginated with silk. Then a posterior gastro-jejunostomy was made, the opening running downwards and to the right, its lower edge being one inch away from the transverse suture line. The opening in the jejunum was about three inches away from duodeno-jejunal flexure, this amount of pedicle being necessary for union without tension. Operation lasted about an hour.

Patient was very little shocked afterwards. Intra-tracheal method of anæsthesia was a great advantage, as the abdomen was quiet. It was, however, rather difficult to close abdomen owing to rigidity of the muscles. Tube containing a wick of gauze was placed at upper end of wound and left for forty-eight hours. A great deal of serum escaped by it. Patient did well although he had a little inflammation of his wound and could take but little food at a time at first, and had a great distaste of all solids. About ten days later a discharge appeared in wound and irritated skin edges. This was acid and was clearly gastric juice. Some mucus also appeared, but no food. Patient was better, however, temperature being normal, and he enjoyed his food more. He was made to lie down flat instead of being in sitting-up position, with the result that the discharge rapidly diminished and skin condition improved. In September, 1915, Dr. Carpmael wrote that the patient was "very fit and working as a bricklayer."

CASE 3.—Man, æt. 58. Very anæmic. Death of exhaustion. Patient of Dr. Norman. Patient has had indigestion for about three years, becoming much worse during last three months. He had severe vomiting of coffee-ground material about three weeks ago and also had severe melæna. Dr. Norman found a large pulsating lump in epigastrium. As the growth was mobile, resection was advised in spite of large size of growth and the severe anæmia.

Operation on June 27th, 1913.—Dr. Shipway gave ether intra-tracheally. Large median incision made in epigastrium extending to two inches below umbilicus. Liver was healthy. There were no nodules of growth on intestine. A tiny nodule was felt in peritoneum of pelvis, but it was doubtful whether this was a growth. The growth in stomach occupied pyloric region and extended more along the greater than lesser curvature. In spite of considerable adhesion to transverse meso-colon, it was decided to attempt removal of growth, for there were no other unfavourable adhesions. The bloodless part of lesser omentum was opened. Pyloric artery was tied and divided, and upper surface of duodenum was cleared for two inches. It was difficult to get gastric artery into view; therefore, it was not tied at this stage. The left gastro-epiploic and great omentum were tied far to the left about four inches beyond growth. It was impossible to isolate right gastro-epiploic owing to adhesion of growth. Great omentum was separated from the left, several bleeding points being tied, and with great difficulty the upper lamina of transverse meso-colon adherent to growth was separated from the middle colic artery, some of the branches of which were opened and tied. A good many

glands were also removed from this neighbourhood. Transverse meso-colon was also separated with some difficulty from growth, and some of its peritoneal surface was taken away with growth. Sero-muscular sutures were then used to close gap. A slice of the anterior surface of pancreas was also removed with growth, and the gastro-duodenal artery was secured and tied. Lower border of duodenum was cleared for two inches, and two clamps were put across it, and duodenum divided. The distal end was closed with a continuous catgut suture passed around the clamp, the two ends of the suture were tied together, puckering the end up, and two sero-muscular sutures, both of which included the pancreas, were used to invaginate stump. Then the stomach was drawn downwards and to the right while a posterior gastro-jejunostomy was performed five inches away from growth. It was very difficult to get stomach into a clamp; therefore, none was used for stomach, but one was used for jejunum. An opening three inches long was made and anastomosis completed in usual way. Then two large clamps were passed across stomach along a line running downwards and well to the left from right border of œsophagus. The left clamp passed across greater part of lower end of œsophagus. The gastric artery had been double ligatured and divided just before this stage. Then without difficulty the opening in remainder of stomach was closed with three layers of sutures, two of catgut and one of fine silk. The first was an ordinary over-stitch, the second a Connell, and the third an ordinary Lembert. Operation lasted an hour and a half, including induction of anæsthetic. There was some delay owing to adhesions already mentioned. Infusion was carried on during and after operation. Patient died marasmic fifteen days later. There was a small fistula at lower end of section of stomach.

CASE 4.—Woman, æt. 60. Recovery; well a year and a half later. Patient of Dr. Lipscomb. Patient was very thin. History of indigestion and vomiting for two years, rapidly getting worse. A palpable and visible movable swelling in epigastrium.

Operation on July 28th, 1914.—Ether was given after morphia and atropine. Incision made through upper part of right rectus. A growth was found in stomach on lesser curvature just reaching pylorus and extending within three inches of œsophagus, and also down anterior and posterior walls for three inches. Enlarged glands were seen in lesser omentum and in great omentum. There was no growth in liver or pelvic peritoneum, and the primary growth and glands were movable; therefore, a resection was carried out. The pyloric, coronary, gastric, and both epiploic vessels were tied, and the borders of duodenum and stomach cleared at points of ligature. The great omentum was detached from the front of transverse colon, and its left and upper corner was tied and divided near spleen. In separating the great omentum several small hard nodules of growth were seen in it below and near to transverse colon. The great and small omenta with their lymphatics were removed in one piece with the stomach. Duodenum was divided one inch from pylorus and closed by a continuous

perforating suture and two purse-strings of linen thread. Stomach was then divided along a line extending from one inch to the right of œsophagus downwards and outwards to lower border so that a pouch about the size of a closed fist was left. The open end of this was then joined to the first part of jejunum, which was drawn up through an opening made for the purpose in transverse meso-colon. Two layers of sutures were used and the opening in transverse meso-colon was closed by two sutures passed between it and the loop of jejunum. Abdomen was closed in layers in usual way. Tube was left at upper angle of wound. The operation lasted one hour. Patient infused four pints into axillæ during operation. She got rapidly well and was in good health eighteen months later.

CASE 5.—Man, æt. about 60. Secondary hæmorrhage a month after operation; death. Patient of Dr. Lewin. Was alcoholic and had mitral regurgitation. Gastric symptoms two years; pyloric stenosis and wasting six months.

Operation on March 22nd, 1915.—Dr. Lewin assisted and Dr. Edmunds gave A.C.E. and ether. Patient had been prepared in the ward for two days, and had had stomach washed out on night previous to operation. Incision was made through upper and inner part of right rectus. Stomach was examined and found to be considerably dilated. There was a hard mass the size of an egg at pylorus, especially on lower border and posterior surface. This was somewhat adherent behind, and there were enlarged glands near it, but no growth could be felt in liver or pelvic peritoneum. It was thought that the swelling was malignant, and Dr. Lewin and I decided to remove it. This was done with some difficulty, for some of the front of pancreas had to be removed with growth, and there was a good deal of bleeding in this neighbourhood. It was also difficult to get duodenal stump up. This was tied with linen thread and then invaginated with a similar thread. Oozing from head of pancreas was stopped partly by tying and partly by sewing. The great omentum was not removed, but was divided close to transverse colon between ligatures. The left gastro-epiploic, gastric and pyloric arteries were tied early in the operation, and gastro-duodenal was tied as it lies behind duodenum, during separation of ulcer from pancreas. Patient was infused during operation several pints. He stood operation fairly well, although he became very pale and lost a fair amount of blood. Amount removed was about a little more than a third of stomach and first inch of duodenum. The anastomosis was made between cut end of stomach and jejunum three inches from its origin. Bowel had been brought up through an opening in meso-colon. This was closed by several sutures joining the edges to stomach and jejunum. Tube containing wick of gauze was placed at the upper angle of wound, which was otherwise closed in layers. The operation lasted an hour and forty minutes. Microscopic examination proved the ulcer to be carcinomatous. A month later patient was going about and getting on well, when he had severe secondary hæmorrhage and died shortly afterwards. The blood issued from a small sinus at site of the drainage tube.

Case 6. - Woman, æt. 55. Recovery; well nine months later. Patient of Dr. Berry of Swindon. Very thin and anæmic. For ten to twelve years has had vomiting and indigestion on and off. Sometimes well for a long time. Much worse last four months, mostly in bed last three months. Six weeks ago had much epigastric pain. Vomit chocolate-coloured. Vomiting two or three times a day. Losing weight rapidly. Appetite fair, but cannot eat even Benger's Food or eggs on account of pain. Lives on milk and biscuit. Constipated. Operation was strongly recommended, but patient preferred to wait. Diagnosis, gastric ulcer, ? becoming malignant.

Operation on April 30th, 1915.—Very large ulcer on lesser curvature near pylorus. This ulcer was becoming malignant. Therefore, two-thirds of stomach and an inch and a half of duodenum were excised in order to get well wide of the disease. Duodenum was closed and jejunum about four inches from its origin was anastomosed to open end of stomach. Catgut was used for deep suture and linen thread for the other. No drainage adopted. Patient stood operation fairly well, and made a rapid and excellent recovery. Microscopic examination by Dr. Nicholson proved the carcinomatous nature of growth. Dr. Berry wrote on September 11th, 1915: "In reply to your letter re Mrs. S., upon whom you operated for carcinoma of stomach, I am pleased to say she is very well indeed; looking and eating well. Mrs. S. says she thinks it must all be a dream and that she will wake up one day to find she has her old trouble after all."

Case 7.—Man, æt. about 60. Death of shock. Patient of Dr. French. Looked anæmic and ill, and had very marked pyloric obstruction.

Operation on June 1st, 1915.—Abdomen explored with a view to gastro-enterostomy, but large hard ulcer found at pylorus and extending along lesser curvature nearly to œsophagus. I thought this was malignant and also that it was removable. There were no secondary growths in liver or peritoneum. I therefore removed the greater part of stomach, having tied all vessels first so as to avoid hæmorrhage, of which there was very little. I joined the jejunum to the opening in cardiac end of stomach. Operation lasted about an hour. Patient was considerably shocked during operation, and in spite of infusion died that night.

Case 8.—Mr. T., æt. 48. Patient of Dr. Morgan Owen. Death of shock. Patient was thin, anæmic, and exhausted, and had a large movable pyloric tumour.

Operation on July 19th, 1915.—Gastrectomy was done in usual way, but patient died of shock about three hours after operation. He took the anæsthetic very badly, and it was thought that he would die on the table. Time, 75 minutes. Although he was infused, he never regained consciousness.

CASE 9.—Mrs. E., æt. 41. Recovery. Patient of Dr. Brackenbury. Patient had suffered increasingly from indigestion for three years. Recently she had hæmatemesis and had wasted rapidly. She often vomited large quantities. Radiography revealed pyloric obstruction. I had felt a tumour of moderate size in epigastrium a little to right of middle line, and patient looked ill and anæmic, was vomiting large quantities about once a day, and was unable to take more than liquids. I therefore advised operation.

Operation on August 21st, 1915.—Dr. Brackenbury present. Long incision made in epigastrium to right of middle line. A dilated stomach, hypertrophied and œdematous, found, and a pyloric ulcer of large size extending halfway along lesser curvature from pylorus around which it formed a ring, which was hard and felt like carcinoma. As stomach was particularly movable and there were no growths in liver or pelvic peritoneum or glands, I decided to resect diseased part, and this was done without delay. The gastric artery was double ligatured and divided, the left gastro-epiploic also, then the great omentum close to transverse colon, and the right gastro-epiploic and pyloric arteries. Duodenum crushed one inch beyond pylorus and sealed with a running suture of linen thread, and then invaginated by two purse-strings of same material. A loop of jejunum brought up through transverse meso-colon and sewn to back wall of stomach along a selected line a little on cardiac side of middle of stomach. Thick black thread was used. Then stomach was divided near line already mentioned between two clamps so that no leakage occurred. An opening the same size as the one in stomach made in jejunum, and an anastomosis made as in gastro-jejunostomy, black thread being used throughout. The sewing of jejunum to stomach before growth was removed greatly facilitated operation, for the growth was useful as a tractor, and later on the attachment to jejunum prevented retraction of stomach during insertion of deep suture. The opening in jejunum began four inches from end of duodenum and by starting it here there was no tension upon first part of jejunum and duodenum. Only two layers of sutures were used for anastomosis. The great omentum not removed, but drawn up over the anastomosis and stump of duodenum. Opening in transverse meso-colon closed by two interrupted sutures. Operation lasted forty-five minutes, and patient was not shocked after it. She was infused during operation, two pints being run into armpits. Very well next day, but vomited once or twice. On the 23rd she frequently vomited small quantities of offensive green material, and as half-a-pint of Sod. Bicarb. solution was given without affording any great relief, the stomach was washed out at 5 p.m., a very large quantity of bilious liquid being withdrawn with great relief. Patient up on tenth day and walking about on thirteenth day and eating almost full diet. She rapidly gained weight and did very well.

CASE 10.—Man, æt. about 60. Pneumonia; death. Patient of Dr. Mutch. Patient referred to me by Dr. Mutch with a diagnosis of carcinoma of stomach. Had been examined with X-rays, which showed py-

loric obstruction. Chemical examinations showed altered blood and deficiency of HCl. Patient had wasted a good deal and was vomiting large quantities. When I saw him at Out-Patients visible peristalsis very obvious in a large stomach. I advised operation without delay. A small tumour could be felt to left of middle line in epigastrium. This moved pretty freely.

Operation on November 9th, 1915.—Very long incision made to right of middle line in epigastrium. Liver and peritoneum normal. No effusion. A growth at pylorus, movable, with many enlarged glands, especially along lesser curvature, extending almost to œsophagus. Resection decided upon and carried out with some difficulty owing to glands mentioned, and also to adhesion between growth and transverse meso-colon, most of which had to be sacrificed, leaving middle of colon somewhat poorly supplied with blood. Three-quarters of stomach removed, and early jejunum joined to cut section of stomach with some difficulty at upper end of anastomosis. Opening in transverse meso-colon closed with sutures, which somewhat angulated colon. Good deal of oozing from head of pancreas, some of which had to be removed with the growth. Therefore, tube left in at upper end of wound. Good deal of oozing of blood continued there next day. Patient was doing very well on November 11th. Had not been sick at all since operation, but he died of pneumonia two days later.

CASE 11.—Man, æt. 63. Recovery. Patient of Dr. Shaw. The X-rays and chemical examinations suggested gastric carcinoma (pylorus). A swelling was felt in the left epigastric angle. The patient was thin and very pale although he had had no severe bleeding; only coffee-grounds vomit at times. Therefore I did not think that the case was a hopeful one for resection. On pelvic examination no secondary growths could be felt.

Operation on June 9th, 1916.—A long incision was made in the left epigastric angle. A growth the size of a fist was discovered at the pylorus, freely movable. No obvious enlargement of glands and no secondary growths in the peritoneum, liver, or portal fissure could be found. Therefore, I rapidly removed the growth and joined the side of the jejunum four inches from the duodenum to the open end of the cardiac portion of the stomach. The operation lasted fifty minutes, and the patient was not materially shocked. The greater parts of the lesser end of the gastro-colic omenta were removed together with their lymphatic glands. Preliminary ligature of the main vessels of the stomach made the operation almost bloodless. The patient did very well and rapidly gained weight.

COMMENTS.

These 11 cases are all the cases of carcinoma of the stomach in which the growth has been resected by the writer between November, 1909, and June, 1916. Many patients have come too late

for any operation to be undertaken, the signs of secondary growths or hopeless marasmus being so evident that exploration was contra-indicated. In many instances exploration has shown resection to be impossible, but in a few of these pyloric obstruction has been so marked that a short circuit has been performed with great relief and prolongation of life for some time, in one instance as long as two years. Some of these patients have gained several stone in weight, and have improved so enormously in general health that the diagnosis of growth has been in doubt for some time. In the majority, however, only a very temporary relief has been obtained. Therefore, the writer has been very keen to resect the growth whenever possible, believing this to be in the best interest of the patient, even when the risk appeared great owing to the advanced state of the disease.

In every case the specimens removed were very carefully examined, nearly all of them by Dr. Nicholson, the Surgical Pathologist at Guy's, microscopically, and showed conclusive evidence of malignant disease. In the majority the clinical and pathological evidence pointed very strongly to the supervention of malignant upon simple ulceration, and in several instances sections from some parts of the ulcer only revealed inflammatory changes, whereas in other parts carcinoma was only too evident.

Mortality.

Five out of the 11 cases died as a result of the operation, two of shock, one of pneumonia, one of secondary hæmorrhage five weeks after operation, and one of exhaustion at the end of a fortnight. All these cases were known to be risky before the operation, for four of them were thin, anæmic, and exhausted as a result of hæmorrhage, malnutrition, and too long delay before the operation. The fifth was a chronic alcoholic with mitral disease so imperfectly compensated that one physician had advised against any operation, but another had recommended an operation later on, when things were getting desperate. The operation proved very difficult, and the patient was very ill for

suddenly a secondary hæmorrhage proved fatal. On the other hand, Case 1 seemed to be desperate before operation, but the patient recovered and worked for over four years before recurrence laid him low.

From these cases it appears to be of the greatest importance to prepare the patients well before operation, and to infuse them before, during, and after the operation. It also appears to be unwise to use unabsorbable thread for the deep suture, for the separation of this led to the fatal secondary hæmorrhage in Case 5. It is certain that the difficulty, duration, and risk of the operation increase very greatly with the delay before the operation. Contrast in this connection Case 9, in which the operation was early and easy and only took 45 minutes, with Case 5, in which the operation was late and difficult, taking nearly two hours. The mortality will be very greatly reduced when patients are sent earlier for operation.

Recurrence.

The cases are few and the time since the operation short in some of the cases, but so far in only one of the six who survived the operation is recurrence known to have taken place, but this was at the end of four years, showing how long cancer cells may remain latent in this neighbourhood.

In Conclusion.

The writer is greatly impressed with the value and need of early operations in these cases of cancer of the stomach. In most cases an exploration is necessary to establish the diagnosis early enough for a hopeful resection to be undertaken. As will be seen the writer has used several methods of resection, and as a result of his experience he is now convinced that the one he recommends in the text is by far the best method he has yet tried. To join the side of the first loop of the jejunum to the open end of the cardiac remainder is a great advance, making the operation much easier, safer, and quicker.

The writer wishes to acknowledge his great indebtedness to the Drs. Mayo for the priceless inspiration and stimulation of their work, and to Messrs. Churchill for their permission to use the figures, which were drawn for the 6th edition of "The Operations of Surgery" (Jacobson). The writer has modified and added to his account of partial gastrectomy which appeared in that edition, and especially he has thought it wise to give details of all his own cases, for such a series often gives a very intimate idea of the value of an operation in actual practice, when the interest of the patient is considered paramount, and without too much regard to the mortality.

Partial Gastrectomy for Carcinoma of the Stomach.

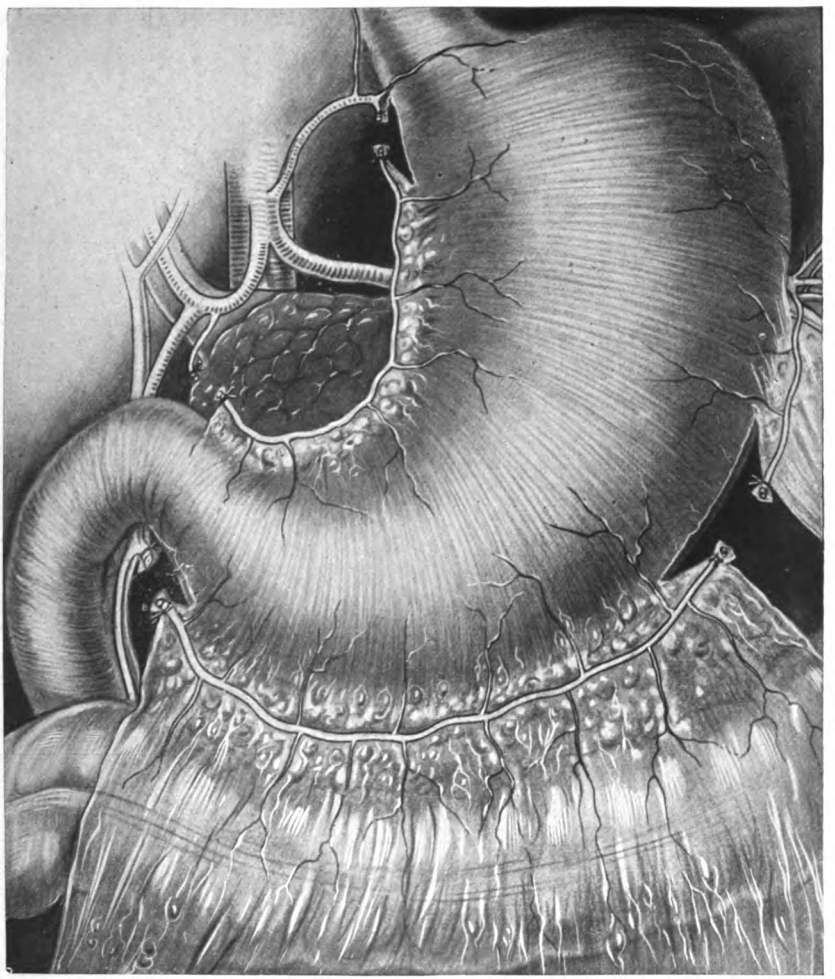


FIG. 1.

Partial Gastrectomy. The large vessels have been tied and the borders of the stomach cleared ready for the clamps.

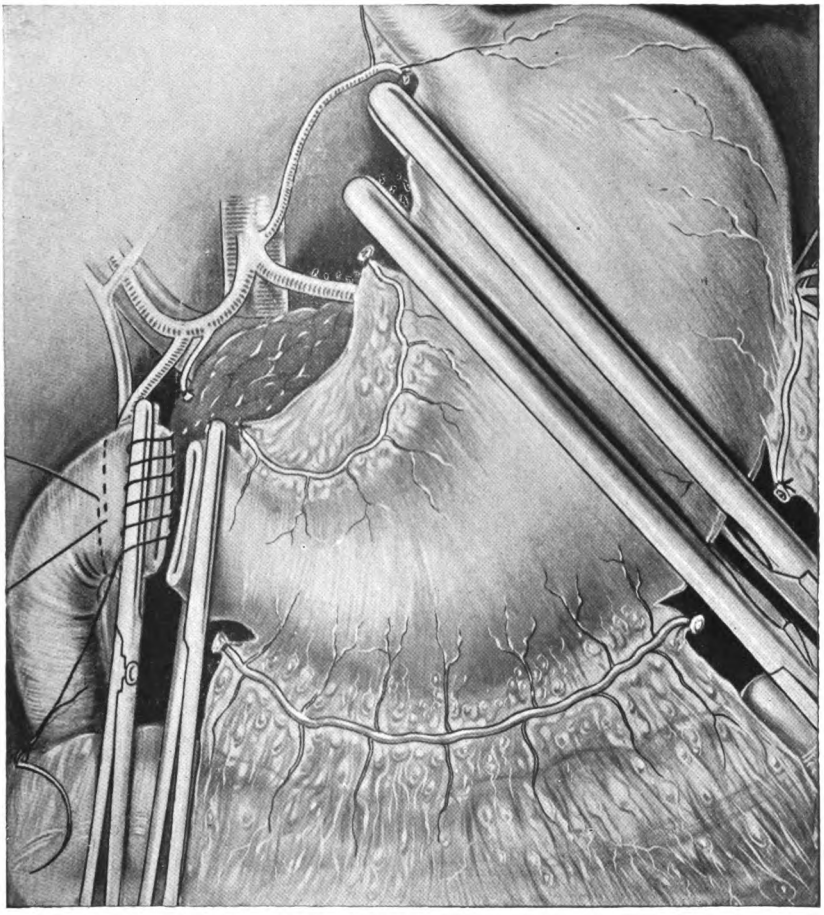


FIG. 2.

Partial Gastrectomy. Clamps applied and the duodenum divided. The duodenal stump is seen over the blades of the clamp holding it. As the clamp is withdrawn the suture is tied. A purse-string suture is also shown.

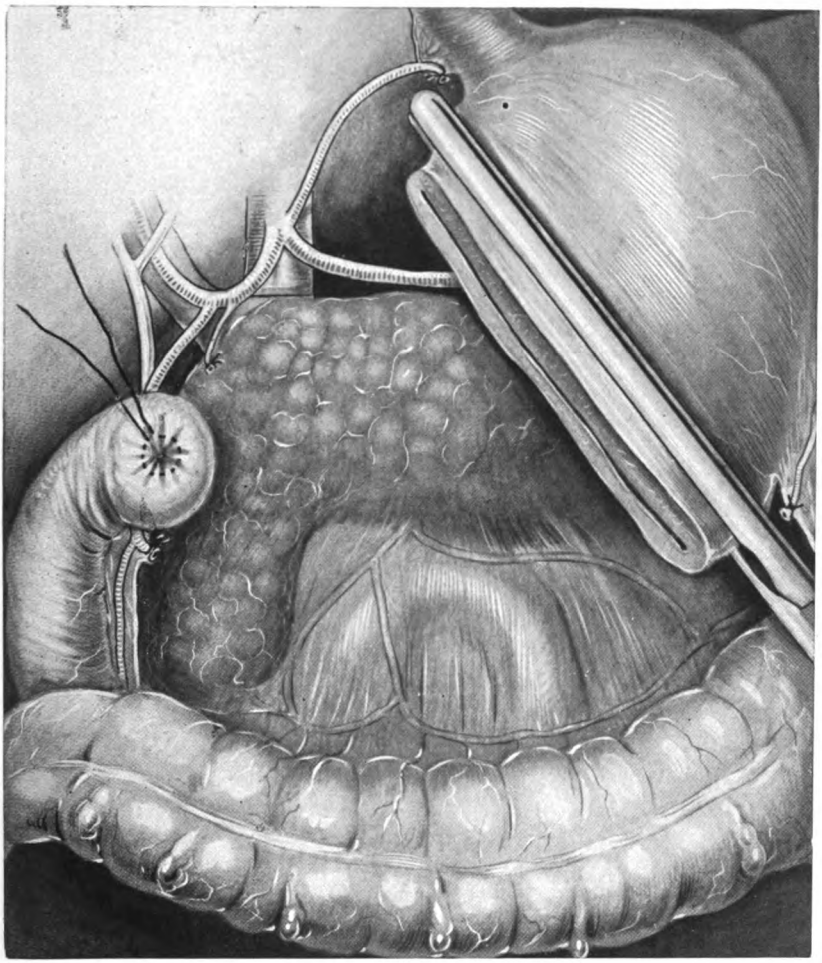


FIG. 3.

Partial Gastrectomy. The growth has been removed, and the duodenal stump closed. The transverse meso-colon and its vessels are shown undamaged.

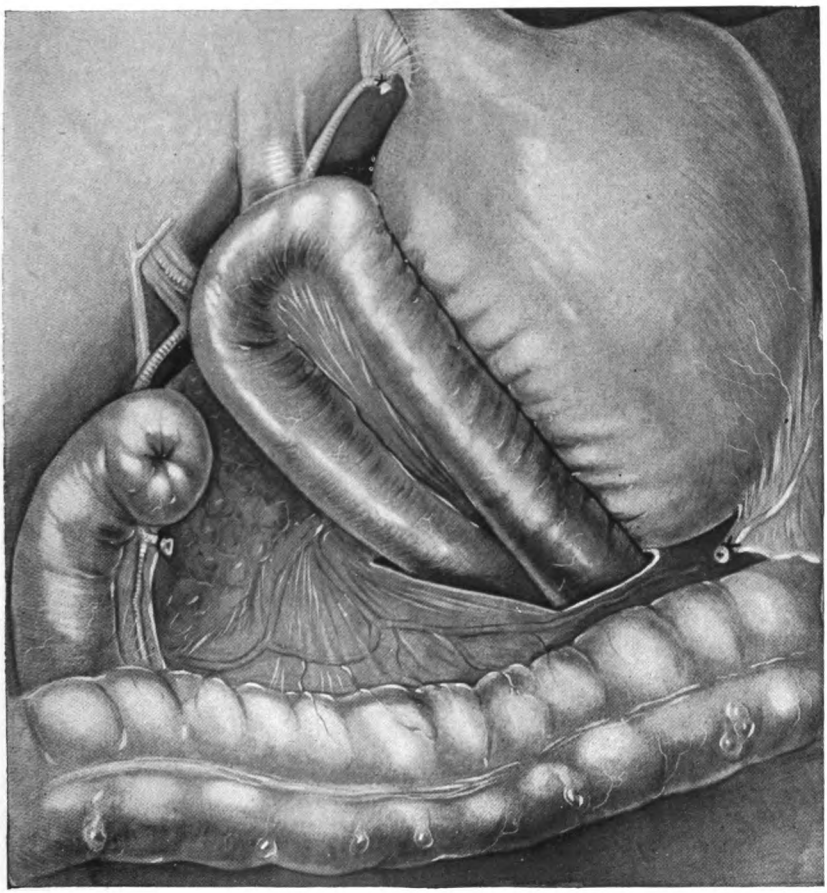


FIG. 4.

Partial Gastrectomy. The jejunum is joined directly to the opening in the cardiac remainder of the stomach.

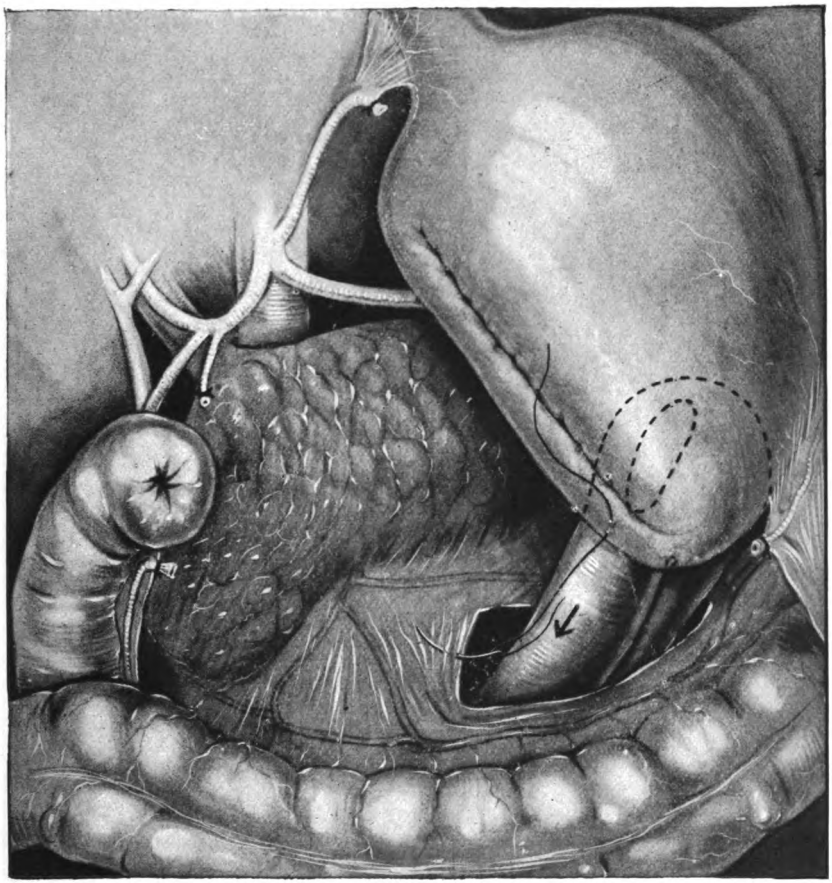


FIG. 5.

Partial Gastrectomy. The cardiac opening has been closed and a gastro-jejunostomy performed. This, the old method, is not so satisfactory as that shown in Fig. 4.

THE COMPLUETIC REACTION (WASSERMANN) IN AMENTIA: AN ORIGINAL STUDY OF 100 CASES.*

By

H. F. STEPHENS.

All the experiments for this investigation were carried out by me in the Bacteriological Laboratories at Guy's Hospital, and my thanks are due to Dr. Eyre, the Director, for having placed every facility at my disposal, and to Dr. Ryffel, the Chemical Pathologist, for his advice and assistance. I am also indebted to my Board of Management and to my Medical Superintendent, Dr. Caldecott, for their courteous permission to undertake this investigation in the case of patients resident under their care at the Royal Earlswood Institution, at Redhill, in Surrey.

A foreword is, perhaps, necessary in explanation of the title. By the "compluetic reaction" I mean the "Wassermann reaction." It ought never to have been called the "Wassermann reaction," for, as everybody should know, not Wassermann but the Belgian Professor Bordet was the first to "discover," to study and "establish" the essential principle of the test. As England to-day is at war for justice and fair play, it is only meet and right and, perhaps, our bounden duty that the Belgian should come to his own again! The proper name for the "Wassermann reaction" is the "Bordet-Gengou phenomenon in syphilis," but, although this is rightly its proper name, such a designation, however romantic the association of the things dis-

* A paper read before the Psychiatric Section of the Royal Society of Medicine on May the 30th, 1916.

covered with the names of their discoverers may be, is nevertheless not quite correct. For it is but a mere truism to maintain that natural processes exist and are not made; they always were and will be, in spite of their discoverers; and it is with the things themselves that science is concerned. The more correct phraseology, therefore, would be "the complement-fixation or deviation phenomenon in syphilis." For this rather cumbrous expression I have taken the liberty to make the simpler term the "compluetic reaction," coining the word "compluetic" from the two words "complement" and "luetic."

This paper is divided into two sections:—

(A) A summary of the technique employed in the experiments.

(B) An analysis of the results obtained thereby.

(A) The Technique Employed.

The technique employed was that in current use at Guy's Hospital. It may be briefly summarized under the following three heads:—

1. The reagents used in the test.
2. The preliminary preparations for the test.
3. The test.

The Reagents.

As is well known, the reagents required for this test are:—

1. Antigen.
2. Reagin (blood serum or cerebrospinal fluid).
3. Complement.
4. Hæmolysin.
5. Erythrocytes.
6. Saline solution.

The materials used in my experiments were as follows:—

1. For *antigen* a 1 in 10 saline solution of an alcoholic extract of human congenital syphilitic liver.
2. For *reagin* only the blood sera were used. The sera were obtained from the peripheral blood of the patients. They were used undiluted.

3. For *complement* a 1 in 10 saline dilution of fresh guinea-pig's serum.
4. For *hæmolysin* a ,1 in 20 saline dilution of the hæmolytic sera of rabbits immunised against human red blood corpuscles.
5. For *erythrocytes* a saline suspension of fresh human red blood corpuscles, obtained always independently of the bloods to be examined, and diluted 100 times (1 in 100).
6. A 0·9 per cent. *saline solution,* freshly made and sterile, was used for all dilutions in the test.

It may not be out of place here to note the following facts concerning the reagents :—

1. *Antigen.*—The strength and properties of a good antigen tend to remain constant. Its characteristics must, however, be redetermined and confirmed from time to time by testing the antigen against known syphilitic reagins. This practically consists in the performance of a test in which all the factors are known except the strength and properties of the antigen. The antigen used in my experiments had been used in the routine performance of many thousands of tests, in all of which it was proved to be neither hæmolytic nor anticomplementary, but truly antigenic in its properties.

2. *Reagins.*—These were always tested against and compared with known "positive" and "negative" sera as "controls."

3. *Complement.*—As is now fully recognised, the complement is the most important factor in this reaction, but unfortunately it tends to degenerate very easily. The strength of the complement, therefore, varies, and must be determined daily immediately before the tests are performed. The strength of the complement is best expressed in the terms of what is known as the minimal complementary dose (the "M.C.D."), the daily determination of which is one of the preliminary preparations for the test and will be described later. By means of the M.C.D. a scale of gradations can be obtained whereby what may be a purely qualitative test can be converted into a quanti-

tative reaction. At Guy's Hospital both the qualitative and quantitative methods are in daily use. In every one of my cases, however, two minimal doses of complement were always employed, for by experiment I found that both from the qualitative and quantitative standpoints two minimal complementary doses were sufficient for each of my cases, a greater dosage resulting in the presence of an excess of complement, and, therefore, in the production of error. It is necessary to emphasise the amount of complement employed, as the results with this test from the quantitative standpoint are only of value when expressed in terms of the M.C.D., from which it follows that, in my series of cases, even the definitely positive reactions are quantitatively very feeble.

4. *Hæmolysin.*—The hæmolysin tends to remain constant. The strength of the hæmolysin is also best expressed in terms of what is known as the minimal hæmolytic dose (the "M.H.D."). The M.H.D. for any given brand of hæmolysin therefore tends to remain constant. The M.H.D., however, should be confirmed from time to time in the manner of the method described later.

The Preliminary Preparations.

The compluetic test, it will be remembered, is an attempt to ascertain whether a given serum in the presence of syphilitic antigen is able to "fix" complement, that is, to de-ionize it, to rob it of its oxydases, and so to render it inactive. The test is not only a means of ascertaining whether a given serum can "fix" complement, but also how much complement it can so render inactive. The test is, therefore, both qualitative and quantitative. It is a means of ascertaining not only the *fixation ability,* but also the *fixation capacity* of the tested serum.

Now in order to be able to "fix" complement, the given serum must contain syphilitic reagin, *i.e.*, the syphilitic "antibody." Therefore, the test becomes limited to ascertaining whether a given serum contains syphilitic reagin, and if so, the quantity of syphilitic reagin it contains. Thus, in my series of cases, I

was able to determine that a certain proportion of the sera examined did contain syphilitic reagin, and that the reagin so contained was invariably in small quantities, being always enough to utilise two minimal doses of complement. To effect these determinations, the method employed is:—

1. To free a given serum of any complement it will naturally contain, *i.e.*, to "inactivate" it.

2. To add to a measured quantity of the inactivated serum a measured quantity of antigen.

3. To add to this mixture a measured quantity of fresh complement.

4. A certain specified time is then allowed for these three substances to interact, and at the end of this time, *i.e.*, usually after one hour in the air incubator at 37° C., the presence of "free" complement is looked for by means of a delicate "colour indicator." If "free" complement is then found to be present, the serum does not contain syphilitic reagin, and is said to be "negative." If, however, "free" complement is found to be absent (the added complement being "fixed"), the serum does contain syphilitic reagin and is said to be "positive"; the degree of its "positivity" being determined by the quantity of added complement that has been "fixed."

Such is the test. Its practical value depends upon the delicacy of the "colour indicator," whose efficiency, in its turn, is dependent upon its ability to detect the smallest traces of complement. Therefore, it will be seen the preliminary preparations for the test are three in number:—

1. The preparation of the reagin.

2. The preparation of a delicate colour indicator.

3. The determination of the smallest amount of complement that can be detected by means of this "colour indicator."

These preliminaries will now be considered.

The Preparation of the Reagin.—In all my cases each specimen of blood for examination was taken from the peripheral circulation, about 5 c.c. of blood being withdrawn with aseptic

precautions from the median basilic vein. Each specimen was allowed to clot, and the serum collected. The serum was then divided into two equal portions. One portion was heated by being placed in a hot-water bath at 56° C. for half an hour (*i.e.*, "inactivation by heat"). The other portion was kept at room temperature for four days before being tested (*i.e.*, "inactivation at room temperature"). The reason why each serum was divided into two portions, one being heated, the other not, is as follows: Every syphilitic serum is supposed to contain two substances, complement and syphilitic reagin (antibody); "inactivation by heat" eliminates the complement, leaving reagin for the purposes of the test. But many workers at Guy's Hospital in a long experience of many thousands of cases have found that heat also tends to damage these syphilitic reagins, some more intensely than others, so that a possibly positive serum may declare itself as negative. It has, therefore, been the practice at Guy's Hospital in all cases of doubtful reactions to re-test the serum, unheated, and after keeping for four days at room temperature. In my 100 cases, however, I have methodically pursued the double course, systematically dividing each serum into two equal portions, and regularly examining these after "inactivation by heat" and after "inactivation at room temperature." The outcome of this procedure has been that the results differed in fourteen of my 100 cases. Of these fourteen cases, four were negative heated, weakly positive unheated; ten were negative heated, definitely positive unheated. The results in all the other cases agreed both with the heated and the unheated portions of the sera. By testing the unheated sera in every case I was able to confirm the results obtained with the heated sera, and vice versa. Against the method of "inactivation at room temperature" it might be urged that normal sera tend to become positive on keeping, because of the factor of hydrolysis, which will naturally set free fatty and amino acids in the serum, an excess of such molecules having a decided anti-complementary action. But such a tendency would have been present in every one of the 100 sera examined, and yet in only

fourteen cases did the results differ. Moreover, all these fourteen cases did not occur on the same day, under the same conditions of atmospheric pressure and temperature; and a further examination of the records showed that one occurred in a set of four, two occurred in a set of five, two occurred in a set of eight, four occurred in a set of eight, one occurred in a set of twelve, one occurred in a set of thirteen, and three occurred in a set of fourteen. So that the factor of hydrolysis does not seem wholly to explain why under the same conditions more positive results should not have occurred.

The Preparation of the "Colour Indicator."—In the preparation of a delicate "colour indicator" for this test, advantage is taken of the well-known fact that in the presence of complement and hæmolysin red blood corpuscles are destroyed, the hæmoglobin escaping to colour the medium; but that in the absence of complement no hæmolysis occurs. On the basis of this fact a mixture of hæmolysin and erythrocytes is prepared. By this mixture the hæmolysin combines with the red cells and is said to render them "sensitive" to complement. The mixture is, therefore, called "a suspension of sensitised erythrocytes." In the actual making of the "sensitised erythrocytes" two stages occur: (1) The determination of the minimal dose of hæmolysin that with complement will produce in a definite period complete hæmolysis of the smallest convenient quantity of red cells; (2) the mixing of the components in these proportions.

The Determination of the Minimal Hæmolytic Dose.—The reagents required for this determination are: (1) a 1 in 20 saline dilution of hæmolysin; (2) a 1 in 100 saline suspension of fresh human erythrocytes; (3) a 1 in 10 saline dilution of fresh guinea-pig's serum; (4) saline solution (0·9 per cent.). The method is as follows: A series of small test-tubes are taken, marked A, B, C, etc. Into each of these are placed diminishing quantities of the diluted hæmolytic serum, thus: 0·10 c.c., 0·08 c.c., 0·06 c.c., etc. Then 0·50 c.c., the smallest convenient quantity, of the erythrocyte suspension is added to each tube, followed

by the addition of an excess of complement, usually four minimal doses. Each tube is then filled with saline to a total volume of 1 c.c. The following example is appended as an illustration:—

	Test-tube A	Test-tube B	Test-tube C	Test-tube D
Hæmolysin (1 in 20) ...	0·10 c.c. ...	0·08 c.c. ...	0·06 c.c. ...	0·04 c.c.
Erythrocyte suspension (1 in 100)	0·50 „ ...	0·50 „ ...	0·50 „ ...	0·50 „
Complement (1 in 10), four doses	0·20 „ ...	0·20 „ ...	0·20 „ ...	0·20 „
Saline solution (0·9 per cent.)	0·20 „ ...	0·22 „ ...	0·24 „ ...	0·26 „
	1·00 c.c.	1·00 c.c.	1·00 c.c.	1·00 c.c.

The tubes are placed in the air incubator for one hour at 37° C. The minimal hæmolytic dose (the "M.H.D.") is the minimal amount of hæmolysin giving complete hæmolysis of 0·5 c.c. of erythrocytes after incubation in the air incubator for one hour at 37° C. In the above example the minimal amount of hæmolysin producing complete hæmolysis was found to be 0·08 c.c. (in test-tube B). Therefore the M.H.D. for the 1 in 20 saline dilution used was taken as 0·08 c.c.

The Preparation of "Sensitised Erythrocytes."—In the preparation of the "sensitised erythrocytes" used in my tests, four minimal doses of the 1 in 20 saline dilution of hæmolysin were taken for each 0·5 c.c., of the 1 in 100 suspension of red cells. These proportions were used because in actual practice an excess of hæmolysin is found to be necessary on account of the varying numbers of red cells in each 0·5 c.c. of suspension, the varying capacity of the cells for combining with hæmolysin, etc. Thus, if the M.H.D. were 0·08 c.c., the recipe for the preparation would be written as follows :—

℞ Erythrocyte suspension (1 in 100)	0·5 c.c.
Hæmolysin (1 in 20), four times 0·08 c.c. (the M.H.D.)...	0·3 „
	0·8 c.c.

Mix as much as is required in these proportions, and let the suspension stand at room temperature for fifteen minutes at least. For each dose of "sensitised erythrocytes" 0·8 c.c. of the above mixture is used.

The Determination of the Minimal Complementary Dose.—The "colour indicator" having been prepared as above, the

next step is to find the smallest quantity of complement that will produce complete hæmolysis in a definite time of the estimated dose of "sensitised erythrocytes." The reagents required for this determination are: (1) a 1 in 10 saline dilution of the complement to be tested; (2) "sensitised erythrocytes"; (3) saline solution (0·9 per cent.). The method is as follows: A series of small test-tubes is taken, marked A, B, C, etc. Into each of these tubes diminishing quantities of the diluted complement are placed, thus: 0·09 c.c., 0·07 c.c., 0·05 c.c., etc., and then to each tube the dose of "sensitised erythrocytes" already estimated is added. Each tube is then filled with saline to a total volume of 1 c.c. The following example is appended as an illustration:—

	Test-tube A	Test-tube B	Test-tube C	Test-tube D
Complement (1 in 10) ...	0·09 c.c....	0 07 c.c....	0·05 c.c....	0·03 c.c.
"Sensitised erythrocytes"	0·80 „ ...	0·80 „ ...	0·80 „ ...	0·80 „
Saline solution (0·9 per cent.)	0·11 „ ...	0·13 „ ...	0·15 „ ...	0·17 „
	1·00 c.c.	1·00 c.c.	1·00 c.c.	1·00 c.c.

The tubes are placed in the air incubator for one hour at 37° C. The minimal complementary dose (the M.C.D.) is the minimal amount of complement giving complete hæmolysis of 0·80 c.c. of "sensitised erythrocytes" after incubation in the air incubator for one hour at 37° C. In the above example the minimal amount of complement producing complete hæmolysis was found to be 0·05 c.c. (in test-tube C). Therefore the M.C.D. for the 1 in 10 saline dilution used was taken as 0·05 c.c.

The Test.

The test itself may now be described. As already stated all the quantities of the reagents used in my reactions are the same as those employed at Guy's Hospital in the routine examination of cases, with the exception of the complementary doses, which did not vary in my tests, two minimal complementary doses being always used, as these were found by experiment to be both necessary and sufficient for each of my cases. The method employed was as follows:—

The Patient's Serum.—(1) For each serum two small test-tubes marked A and B were taken. (2) In each of these tubes

was placed 0·1 c.c. of the patient's serum. (3) To each tube was then added two minimal doses of complement. (4) Into Tube A, but not into Tube B, was finally measured 0·1 c.c. of the antigen. Tube B was thus used as a "control" against Tube A, for as Tube B contained no antigen, one was able to note whether the patient's serum was naturally anti-complementary or not. (5) The volume of fluid in each tube was then brought to the same level by the addition, where necessary, of saline. Both tubes were then carefully shaken so that the contents of each were well mixed, the completest asepsis being observed in all the measurements.

The "Control" Sera.—Each patient's serum was always tested against and compared with two known sera, a syphilitic and a non-syphilitic serum, used as "controls." For each of these "control" sera two tubes were always prepared similar in every way to the two tubes containing the patient's serum.

For the testing of each patient's serum, then, six tubes were prepared—two for the patient's serum, two for the syphilitic serum, and two for the non-syphilitic serum. When these were ready they were placed in the air incubator for one hour at 37° C. The estimated dose of "sensitised erythrocytes" was then added to each tube, and all the tubes were replaced in the air incubator at 37° C. for another sixty minutes. They were carefully examined at regular intervals, and the results finally recorded at the end of the hour.

A note may here be added with reference to the use of "control" sera in my series of cases. All my tests were performed at the same time and on the same days on which the routine Wassermann work of Guy's Hospital was undertaken. I worked side by side with the hospital serologist, and we used the same materials for our reagents. Therefore, in addition to my own "controls," I had the advantage of the hospital's series of tubes (*i.e.*, of those containing two minimal doses of complement) to check my reactions and to confirm the accuracy of my results.

SCHEMA OF THE TEST.

	Unknown Serum.		Syphilitic Serum.		Non-syphilitic Serum.	
	Tube A	Tube B	Tube A	Tube B	Tube A	Tube B
	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.
Reagin (undiluted)	0·10	0·10	0·10	0·10	0·10	0·10
Antigen (1 in 10)	0·10	—	0·10	—	0·10	—
Complement (1 in 10), two doses	0·10	0·10	0·10	0·10	0·10	0·10
Saline solution (0·9 per cent.)	—	0·10	—	0·10	—	0·10
The tubes are placed in the air incubator for one hour at 37° C.						
"Sensitised erythrocytes"...	0·80	0·80	0·80	0·80	0·80	0·80
	1·10	1·10	1·10	1·10	1·10	1·10

The tubes are replaced in the air incubator for thirty minutes at 37° C. They are then examined every ten minutes, and the results finally recorded at the end of another thirty minutes—*i. e.*, one hour after the addition of the "sensitised erythrocytes."

Interpretation of the Results.—The results in my series of cases were recorded as follows: (1) When no hæmolysis occurred the reaction was said to be "definitely positive." (2) When partial hæmolysis occurred the reaction was termed "weakly positive." (3) When complete hæmolysis occurred the reaction was called "negative."

Summary of the Technique.

In their preliminary report on the methods of carrying out this test, the Sub-Committee of the Section of Pathology of this Society defined what is generally understood to be "the original Wassermann test" by its essential principles as follows:—

"(1) The ingredients of the test (red corpuscles, 'antigen,' hæmolytic amboceptor, complement) are derived from *different* sources.

"(2) The serum to be tested is inactivated before use. An independent 'hæmolytic system' is employed, consisting of a

suspension of red corpuscles, an inactivated hæmolytic serum, and a fresh normal serum containing complement. The hæmolytic values of the antiserum and complement are determined by a separate preliminary experiment.

"On general scientific grounds the Sub-Committee is unanimously of the opinion that, since the test is a quantitative reaction the titre of the reagents ought, within practicable limits, to be accurately known."

From the above definition of the "original test" the technique herein described will be seen to differ, but it is sincerely hoped that the results so obtained will not, therefore, be very greatly impaired. One of the principles of the "original method," as stated in the above definition, is that the ingredients of the test should be derived "from *different* sources." If this means "from different individuals," then the technique I employed agrees with that of the "original" test. But if it is intended to mean "from individuals of different species" (*e.g.*, the rabbit, the sheep, the guinea-pig), then the technique I employed does not agree with that of the "original" test, for I used in my "hæmolytic system" human red blood corpuscles (always obtained, it must be remembered, *independently* of the bloods to be examined). Three points in connection with the technique must be recalled briefly, inasmuch as these points are directly concerned with the interpretation of the results obtained.

First, the serum. Each serum to be tested was always inactivated before use. Each serum was divided into two equal portions; one was subjected to "inactivation by heat," the other to "inactivation at room temperature." Each portion was then tested in exactly the same way and the results carefully compared, when it was found that in only fourteen cases did the results differ. In all the other cases the results agreed both with the heated and the unheated portions of the serum. Thus, by testing the unheated sera, in every case the results obtained with the heated sera were confirmed and vice versa. As some observers would maintain that more correct results are obtained by "heat-

ing" the sera, and others by testing the sera "unheated," it was hoped to avoid the fallacies arising from both sources by systematically examining each serum in this way.

Secondly, the amount of complement used in each test. In every one of these determinations two minimal doses of complement were always employed, for by experiment it was found that two minimal complementary doses were necessary and sufficient for each of these cases, a greater dosage resulting in the presence of an excess of complement, and, therefore, in the production of error.

Thirdly, the "controls." Three sets of "controls" were used. (1) Each serum, whether heated or unheated, was always tested with and without "antigen," to determine whether it was naturally anti-complementary, and so to avoid if possible an excess of "positive" results. (2) Each serum, whether heated or unheated, was always tested against and compared with two known sera, a syphilitic and a non-syphilitic, under exactly the same conditions. (3) All these tests were performed at the same time and on the same days and with the same materials as the routine Wassermann work of Guy's Hospital. Therefore, in addition to the above "controls," there was always the hospital's series of tubes (*i.e.*, of those containing two minimal doses of complement) by which to check the reactions and to confirm the accuracy of the results.

(B) The Results Obtained.

In this section of the paper the results obtained by the above experiments are analysed as follows:—

(1) *Total Percentage.*—Of the 100 cases examined, forty-two gave positive reactions. None of the fifty-eight "negative" cases, after a thorough clinical examination, revealed any of the characteristic lesions of syphilis, so that this group of forty-two "positive" cases would seem to include all the patients with syphilitic amentia whose blood serums were examined. Of the forty-two "positive" cases, twenty-two were "definitely posi-

tive," and twenty were "weakly positive." To many workers on this subject these figures would appear to yield a large percentage of "positive" results. The following facts, determined by a closer analysis, must, therefore, be stated:—

(i.) That when the sera were *inactivated by heat,* the reaction was found to be present in twenty-eight cases, being—

"Definitely positive" in ... 22 — 10 = 12 cases.
"Weakly positive" in ... 20 — 4 = 16 cases.
"Negative" in ... ... 58 + 14 = 72 cases.

(ii.) That when the sera were *inactivated at room temperature,* the reaction was found to be present in forty-two cases, being—

"Definitely positive" in ... 12 + 10 = 22 cases.
"Weakly positive" in ... 16 + 4 = 20 cases.
"Negative" in ... ... 72 — 14 = 58 cases.

From which it will be seen—

(*a*) That in eighty-six cases the results *agreed* both with the "heated" and the "unheated" sera, being—

"Definitely positive" in ... ... 12 cases.
"Weakly positive" in ... ... 16 cases.
"Negative" in ... ... 58 cases.

(*b*) That in fourteen cases the results *differed* both with the "heated" and the "unheated" sera, so that—

In ten cases the reaction was "negative" heated,
"definitely positive" unheated;
In four cases the reaction was "negative" heated,
"weakly positive" unheated.

Now those workers who would maintain that heat tends to damage certain syphilitic reagins, some more intensely than others, so that a possibly positive serum may declare itself as negative, would regard the fourteen *differing* sera as yielding more correct results when tested after "inactivation at room temperature," and would, therefore, consider that a "definitely

positive" reaction was obtained in twenty-two cases, a "weakly positive" reaction in twenty, and a "negative" reaction in fifty-eight, their total percentage of "positive" results being 42.

On the other hand, those observers who would urge that normal sera tend to become positive on keeping because of the factor of hydrolysis producing strong anticomplementary bodies, would consider the fourteen *differing* sera as yielding more correct results when tested after "inactivation by heat," and would, therefore, record them as "negative," or at best as being "doubtfully positive," and their total percentage would be 28 (16 "weakly positive," and 12 "definitely positive").

Finally, there would be some observers who would hold that because only two minimal doses of complement were used in each of these determinations, only those cases in which the results were noted as "definitely positive"—*i.e.*, those cases in which absolutely no hæmolysis was observed—should be regarded as "truly positive." These would, therefore, discard the "weakly positive" and "doubtfully positive" cases as being "negative," and their total percentage of "positive" results would be 12, with which I personally am in agreement.

However the above figures may be interpreted, the point I wish to emphasise is this: that the results have been very carefully and accurately recorded; the "controls" have been numerous, strict, and efficient; and that under the conditions of the technique employed, as herein described, these results may be considered to be correct.

(2) *Sex.*—All the cases examined were males.

(3) *Age.*—The youngest of these patients was 12 years old, the five oldest were 51, 52, 52, 73 and 78 years respectively. There were fifty-seven patients between 12 and 21 years of age inclusive, twenty-one between 22 and 30 years inclusive, and seventeen between 30 and 50 years inclusive, so that the majority of the patients were boys. This fact is of some importance, for the compluetic reaction tends to vary with age, as is shown in the following tables :—

TABLE A.—SHOWING THE INCIDENCE OF THE REACTION AT DIFFERENT AGE-PERIODS.

Age-periods.	Number of cases examined.	Number of positive reactions at each age-period	Percentage of positive reactions to cases examined at each age-period.	Percentage of positive reactions at each age-period to total number of positive reactions.
Under 12 years ...	—	—	—	—
12 to 15 years inclusive	19 } 57	7 } 26	36·8 } 45·6	16·67 } 61·9
16 to 21 years inclusive	38 }	19 }	50·0 }	45·23 }
22 to 30 years inclusive	21	8	38·09	19·04
Over 30 years ...	22	8	36·36	19·04

From this table it will be seen:—

(i) That of all the positive reactions obtained, twenty-six (or about 62 per cent.) occurred in patients between 12 and 21 years of age inclusive; while only eight (19 per cent.) occurred in those between 22 and 30 years inclusive, and eight (19 per cent.) in those over 30 years.

(ii) That positive reactions occurred in 45 per cent. of the patients between 12 and 21 years of age inclusive, in 38 per cent. of those between 22 and 30 years inclusive, and in 36 per cent. of those over 30 years of age.

Hence it would seem that the incidence of the reaction tended to diminish as the ages of the patients increased. But a closer study of the cases revealed an interesting modification, which also is indicated in Table A, where it is shown:—

(i) That a larger percentage of positive reactions occurred between the ages of 16 and 21 inclusive than at any other period, viz., 45 per cent.

(ii) That 50 per cent. of the patients between the ages of 16 and 21 inclusive gave positive reactions, while about 37 per cent. of those below 16 years, and about 37 per cent. of those above 21 years, gave positive reactions.

From which it appears that the curve of the incidence of the reaction in aments tends to rise from between the ages of 12

to 15, reaching its maximum height between the ages of 16 to 21 and then gradually falling again as the ages increase.

Again, the intensity of the reaction at different age-periods is shown in Tables B and B[1] :—

TABLE B.—BEING AN ANALYSIS OF THE CASES GIVING "DEFINITELY POSITIVE" REACTIONS.

Age-periods.	Total Number of positive reactions at each age-period	Number of cases giving "definitely positive" reactions.	Percentage of "definitely positive" reactions to the total number of positive reactions at each age-period.	Percentage of "definitely positive" reactions at each age-period to the total number of "definitely positive" reactions.
Under 12 years ...	—	—	—	—
12 to 15 years inclusive	7	6	85·7	27·2
16 to 21 years inclusive	19	11	57·9	47·8
22 to 30 years inclusive	8	3	37·5	13·04
Over 30 years ...	8	2	25·0	8·7

TABLE B[1].—BEING AN ANALYSIS OF THE "WEAKLY POSITIVE" CASES.

Age-periods.	Total Number of positive reactions at each age-period	Number of cases giving "weakly positive" reactions.	Percentage of "weakly positive" reactions to the total number of positive reactions at each age-period.	Percentage of "weakly positive" reactions at each age-period to the total number of "weakly positive" reactions.
Under 12 years ...	—	—	—	—
12 to 15 years inclusive	7	1	14·2	5·0
16 to 21 years inclusive	19	8	42·0	42·0
22 to 30 years inclusive	8	5	62·5	26·3
Over 30 years ...	8	6	75·0	31·5

From these tables it will be seen:—

(i) That all the positive reactions, save one, occurring between the ages of 12 and 15 inclusive were "definitely positive," no hæmolysis being detected in any of the cases.

(ii) That the percentage of "definitely positive" reactions diminishes with the increasing ages of the patients.

(iii) That while there is only one "weakly positive" reaction between the ages of 12 and 15 inclusive, the percentage of such reactions increases with the increasing ages of the patients.

(iv) That if a composite graph were drawn illustrative of both these tables it would appear that the curve of the intensity of the reaction is similar to the curve of the incidence.

From this study, then, of the relationship of the incidence and intensity of the compluetic reaction in aments to the age of the patient, it becomes manifest that the reaction tends to be strongest and most frequent in patients between the ages of 16 and 21, and that it appears to be more frequent and stronger in those below 16 than in those above 21 years of age; but it was not possible to determine exactly how either the incidence or the intensity curves should be drawn, the reason for this failure being shown in Table C. Such curves, however, ought to be realised when a very large number of reliable results have been tabulated and examined.

TABLE C.—SHOWING THE NUMBER OF CASES EXAMINED AND THE NUMBER OF CASES GIVING POSITIVE REACTIONS FOR EACH YEAR OF AGE FROM 12 TO 25 YEARS INCLUSIVE.

Age.	C.	+	±	T.
Under 12 years ...	— ...	— ...	— ...	—
12 years old ...	2 ...	— ...	— ...	—
13 „ ...	2 ...	2 ...	— ...	2
14 „ ...	9 ...	3 ...	1 ...	4
15 „ ...	6 ...	1 ...	— ...	1
16 „ ...	7 ...	1 ...	3 ...	4
17 „ ...	8 ...	3 ...	1 ...	4
18 „ ...	6 ...	1 ...	1 ...	2
19 „ ...	7 ...	2 ...	— ...	2
20 „ ...	4 ...	— ...	2 ...	2
21 „ ...	6 ...	4 ...	1 ...	5
22 „ ...	2 ...	— ...	— ...	—
23 „ ...	6 ...	2 ...	— ...	2
24 „ ...	1 ...	— ...	— ...	—
25 „ ...	2 ...	— ...	1 ...	1

C. = number of cases examnied.
\+ = number of cases giving definitely positive reactions.
± = number of cases giving wcakly positive reactions.

(4) *Social Status.*—The fathers of forty-two of the patients were members of the skilled trades and labourers, thirteen patients were the sons of members of the professions, and thirty were born in the mercantile classes. As these cases were chosen spontaneously and more or less haphazard, it is interesting to remark that the parents of the smallest number of these aments are members of the most highly organised occupations, viz., the professions; and it is also of importance to note that precisely those spheres of industry which have shown little or no manifestations of the social spirit contain the parents of the majority of these syphilities (*vide* Table D).

TABLE D.—SHOWING THE SOCIAL STATUS OF THE PATIENTS EXAMINED.

Occupation of Father.	Number of patients examined.	Number of patients giving positive reactions.
Skilled trades and labourers	42	21
Professions	13	4
Mercantile	30	14
Dead and unknown	15	3

All the 100 patients were born and bred in England (in her cities, towns, and villages) except seven. Of these seven, two were from the Channel Islands, one from the Isle of Wight, one from India, one from Barbadoes, one from Mauritius, and one from Buenos Aires. The boy from Buenos Aires and the boy from the Isle of Wight gave "weakly positive" reactions; the sera of the other five were "negative."

(5) *Life-history.*—The compluetic reaction being an index of existing syphilitic infection and not in the nature of an immunity reaction, the question arises as to whether the infection in this series of cases was an intra-or an extra-uterine one, *i.e.*, whether the syphilis was "congenital" or "acquired."

The fact that the majority of these patients came under institutional discipline and observation at a very early age, and were all of them under due protection when at home or with friends, together with the absence in them of all the physical signs and symptoms of "acquired" syphilis at any period of their lives, tends to dispose of the presence of this type of the disease in

any one of these cases, the likelihood of which under the circumstances would be extremely remote. All the forty-two positive cases may, therefore, be said to be in varying degrees the victims of intra-uterine or "congenital" syphilis. But, save for the ophthalmoscopic and otological conditions, which unfortunately were not determined because of the obvious practical difficulties of such inquiries in aments, the most careful examination of the patients themselves failed to reveal the presence of any of the characteristic lesions of "congenital" syphilis in any one of them, a fact which has also been noticed by Dr. Plaut, of Munich, Major Mott, and other observers.* Nor did a study of the records of the parental and family histories adduce evidence of the disease in any of the parents or their forbears—a fact which is less surprising, for the histories in such cases are notoriously misleading. The compluetic reaction, being the only reliable evidence in forty-two of these cases of their being syphilitic at all, was also the conclusive testimony to the presence of syphilis in either or both their parents.

These observations, based only on the clinical aspects and family histories, agree with those obtained by other workers, who may be divided into two groups: those who recorded their observations before the compluetic reaction was used in the investigation of amentia, and those who have themselves employed the test in such investigations. In 1892 Dr. Shuttleworth with Dr. Fletcher Beach[20] published the results of their examination of 2,380 aments, when clear evidence of inherited syphilis was found in only 1·17 per cent. of their cases; while Dr. Langdon Down[21] detected the stigmata in 2 per cent. of cases; and Dr. Ireland[22] recorded with some surprise that the disease was not concerned in the ætiology of amentia. Sir Jonathan Hutchinson, in a visit to the Earlswood Asylum, was also astonished to find in how few cases there was definite evidence of inherited syphilis, or of a syphilitic family history.[23] Later, however, Dr. Sherlock[24] ob-

**Vide* the Appendices to the Reports of the Royal Commission on Venereal Diseases, printed separately in [Cd. 7475, 1914] and [Cd. 8190, 1916]

tained satisfactory evidence of syphilis in one or other parent in 14·4 per cent. of his ninety cases, and Professor Th. Ziehen, of Berlin, detected the disease in as many as 17 per cent. of aments.[25] Therefore, before the advent of the compluetic reaction the percentage of syphilitic cases, based on clinical evidence alone, was considered to be small. Since the employment of the test, however, a larger number of syphilitic cases has been detected, but the same small percentage of clinical results has been obtained, as shown by the evidence of Dr. Plaut, Major Mott, and others who have used the test. Therefore, one of two conclusions is true: either that the reaction is not associated with syphilis, which in the light of our present knowledge would be considered absurd, or that the more obvious clinical stigmata of syphilis are not found in aments, which, with the testimony of the present and past experience of competent observers to support it, would appear to be correct.

A note may here be introduced on the appearance of the stigmata of "congenital" syphilis in aments. It will be remembered that "congenital" syphilis is an intra-uterine affection, and it will also be recollected that the children of syphilitic parents need not necessarily be aments. So that apart altogether from the fact that certain central nervous systems are peculiarly prone to attack by this virus, the manifestations of "congenital" syphilis would appear to be dependent upon the time of onset of the infection *in utero*, bearing a direct relation to the structural condition of the developing organism. That the majority of congenital syphilitics bear evidences of epiblastic or mesoblastic infection would seem to show that the fœtus is not attacked till late in its development, or, perhaps, that the maternal defences are able to protect it till then. The presence of an earlier neuroblastic infection is manifested by the cases of juvenile general paralysis of the insane, a condition to which any of the preceding cases may succumb, while the earliest embryonic infections would appear to result either in the death of the organism or in arrested development. Thus, consider those cases of "infantilism," free

from all obvious syphilitic stigmata, in which Major Mott has seen in both ovary and testis myriad colonies of the Spirochæta pallida. Similarly retarded development of the other members of the endocrinic glands may be found to be due to the same cause, and how closely the endocrinic system is associated with the central nervous system is daily becoming more manifest. Broadly considered, amentia may, perhaps, be interpreted as a symptom-complex of arrested brain development, such retardation being due either to an inherent inability on the part of the brain cells to grow and evolve, or to the effects of some factor inimical to their perfect fulfilment, such a factor being either traumatic, or toxic, or inflammatory in its appearance. In either case the syphilitic virus may be present as cause or coincidence, *e.g.*, the inherent inability of the brain cells to develop may be due to some occult influence of the virus, or the results of its toxicity may be more recent and pronounced. Our knowledge, therefore, of the "stigmata" of congenital syphilis requires some replenishing. How many, for example, of the so-called stigmata of degeneracy are in reality the stigmata of syphilis? We do not know. Those of the latter, so frequently described and portrayed, are mainly somatic in incidence, originating in fully developed structures (*e.g.*, nodes, scars, the syphilitic wig, interstitial keratitis, etc.). What is seriously needed is a more careful study of the germinal developmental stigmata (mainly microscopical in character), and the signs and symptoms with which these are associated, and by which they are rendered more evident to the naked eye, *e.g.*, as in "infantilism," certain cases of cretinism, perhaps also certain groups of simple aments. In other words, evidences of arrested or deranged and irregular development, if shown to be directly due to the effects of the luetic virus, ought to be regarded as being in themselves "stigmata" of congenital syphilis. Again, what of the bio-chemical stigmata? One of these, surely, is that which has been studied in recent years on such a very extensive scale as the "Wassermann reaction."

To continue with this analysis, the next point to be determined was whether the syphilitic virus acting alone was responsible for the mental defect in these forty-two congenital cases, or whether it attained that end with the assistance of other factors. An analysis of such factors, based on a consideration of the so-called "causes" of amentia, is given in Table E, from which it will be seen:—

(i) That in addition to syphilis certain reputed germinal and somatic defects are together present in seventeen cases; that these germinal defects only are present in seven cases; and the somatic defects only in eighteen cases.

(ii) That in addition to syphilis, fourteen cases have at least one of these reputed defects, fourteen others at least two such defects, and eight have three. One case has as many as six germinal and somatic defects, another has five, and four have each four of such defects. In no case is the syphilitic virus unassociated with at least one of these ætiological factors.

Other points to be noted in Table E are:—

(i) Of the forty-two positive cases the neuropathic diathesis occurs in seventeen. (Of the 100 cases examined a neuropathic inheritance was recorded in only forty-four; so that syphilis was detected in seventeen of the forty-four cases with a neuropathic heredity. Of these seventeen cases the diathesis was recorded in seven in the parental histories only, in six in the family histories only, and in four in both family and parental histories. It appeared in seven cases on the maternal side only, in six on the paternal side only, and in four on both sides. Five of these cases gave family histories of amentia, three of insanity, and two of a "neurotic heredity." Eight of the parents were said to be "neurotic," one is insane, one had a spinal affection and was a cripple, and two died in apoplectic fits.)

(ii) There appears to be no family or parental history of alcohol.

(iii) Tuberculosis is seen to occur in the inheritance of six patients: in the family histories of four, and in the parental histories of three.

(iv) Consanguinity is present in two cases. (In one the parents were first cousins; in the other the paternal grandparents.)

(v) One of the patients, a cretin, has a paternal cousin who is likewise a cretin; and the mother and sister of another patient, also a cretin, have suffered from exophthalmic goitre. Each of these cases also has a neuropathic inheritage, but being instances of a metabolic inheritance as well they are again noted here under a separate heading.

(vi) Adverse mental states of the mother were said to have been present during the fœtal development of five cases, and adverse physical conditions of the mother in three. Six others are the children of aged parents.

(vii) Fifteen are firstborn children; ten of these gave definitely positive reactions, the other five being weakly positive. It is, therefore, very probable that a series of abortions may have preceded the birth of most of these patients, although such a history, unfortunately, was not recorded in any case either as positive or negative evidence.

(viii) Difficult and protracted labour with instrumental delivery is recorded in seven cases (four of which were firstborn children).

(ix) One patient was a premature birth, another was a ten months' baby, and a third is the fifteenth child in his family and the second of twins.

(x) Infantile illness is cited in seventeen cases and infantile head injuries in five.

To what extent must now be considered does the syphilitic virus play its part in producing the mental deficiency in each of these cases? Its exact influence is, of course, difficult to estimate, but from a study of Table E it will be seen:—

TABLE E.—SHOWING THE FACTORS CONCERNED IN THE ÆTIOLOGY OF FORTY-TWO POSSIBLE CASES OF SYPHILITIC AMENTIA.

No. of case.	Genminal Defects.																Somatic Defects.							
	Neuropathic inheritance.			Alcoholism.			Tuberculosis.			Consanguinity.		Aged parents.		Other factors.			Fœtal.			Natal.		Infantile.	
	Ancestral.	Maternal.	Paternal.	Ancestral.	Maternal.	Paternal.	Ancestral.	Maternal.	Paternal.	Maternal.	Paternal.	Maternal.	Paternal.	Ancestral.	Maternal.	Paternal.	Adverse mental states of the mother.	Adverse physical conditions of the mother.	Other factors.	Firstborn.	Difficult labour, instrumental, &c.	Illness.	Injury.
(A) The Ætiological Analysis of the Twenty-two Cases giving "Definitely Positive" Reactions.																							
1	+	..	...	...	...	...	+	+	...	...	..	...	...	...	...	...	...	...	...	+	...	+	...
2	+	+	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	+	...
3	...	..	+	...	...	...	...	...	...	...	...	...	...	+a	...	...	+	...	...	...	...	...	+
4	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	+	+	+	...
5	+	+	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	...	...	...	...	...
6	...	+	...	..	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	...	...	+	...
7	...	...	...	...	...	...	+	...	...	...	...	...	...	...	...	...	...	...	...	+	+	...	...
8	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	+	...	+	...
9	+	...	+	...	...	...	...	..	...	+	...	...	...	...	..	...	...	...	...	...	...	...	...
10	...	...	+	...	...	...	...	...	...	...	...	+	+	...	...	...	...	...	...	...	...	...	...
11	...	...	+	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	...	...
12	...	...	...	...	...	...	+	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+
13	...	...	...	...	...	...	...	...	...	...	..	+	+	...	...	...	...	...	...	...	+	...	...
14	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	+	...	...
15	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	+	...
16	...	...	...	...	...	...	..	...	...	...	...	...	...	...	...	...	...	...	+b	...	...	+	...
17	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+c	...	...	+	...
18	...	...	...	...	...	...	...	...	...	...	...	+	+	...	...	...	...	...	...	...	...	...	...
19	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	...	...
20	...	...	...	...	...	.	...	...	...	...	...	..	...	...	...	...	...	...	...	+	..	...	...
21	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	+	...	...
22	...	..	...	...	...	...	..	...	..	...	...	...	...	...	...	...	...	...	...	...	+	...	...

(B) The Ætiological Analysis of the Twenty Cases giving "Weakly Positive" Reactions.

23	±	±	...	...	...	...	±	...	...	...	±	...	...	...	...	...	±	...	...	...	...	±	...
24	±	...	...	...	...	...	...	...	...	...	...	±	±	...	...	...	...	...	±d	...	...	±	...
25	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	±	...	...
26	...	±	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
27		±	...	...	...	...	...	...	...	...	...	±	±	...	...	...	±	...	...	...	...	...	...
28	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
29	...	...	±	...	...	...	...	...	...	...	...	...	...	...	±e	...	...	...	...	...	...	...	...
30	...	...	...	...	...	...	...	±	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...
31	...	...	...	...	...	...	...	...	...	...	...	±	±	...	...	...	...	...	...	...	...	±	...
32	...	...	...	...	...	...		...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	±
33	...	...	...	...	...	...	...	...		...	...	...	...	...	...	...	...	...	...	±	...	±	...
34	...	...	...	...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	±
35	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
36	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
37	...	...	...	...	...	...	...	...	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...
38	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...	...	...	...
39	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...
40	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
41	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
42	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±

a = a cretin whose paternal cousin is also a cretin.

b = a premature birth.

c = a ten months' baby.

d = the fifteenth child and the second of twins.

e = a cretin whose mother and sister had exophthalmic goitre.

N.B.—The sera of all cases printed in italics were *negative* when "heated."

(A) That the virus is undoubtedly an *auxiliary* and *augmentary* factor in the ætiology of eleven cases—viz., in Nos. 1, *2*, 3, *6*, 11, *23*, 24, 25, 26, 28, *29*.

(B) That it probably is the *exciting* or *determinant* factor in six cases—viz., in Nos. 5, *9*, 10, 27, 35, *36*.

(c) That it appears to be the *essential* factor in twenty-five cases—viz., in Nos. *4*, 7, *8*, *12*, 13, 14, 15, 16, *17*, *18*, 19, *20*, *21*, 22, 30, 31, 32, 33, 34, 37, 38, *39*, 40, 41 and 42.

(D) That in no case is it the *only* ætiological factor, for even on analysing group (c) it will be seen:—

(*a*) That though in two cases (viz., *18* and 37) the syphilis appears to be wholly responsible for the amentia, it in reality has produced the mental defect by acting upon already degenerated germ plasm. Thus in No. 37 the boy's father was said to have died of phthisis; and No. *18*, a Mongolian idiot, was the son of aged parents, being the eleventh child.

(*b*) In all the other twenty-three cases, the syphilis appears to be associated with damaged nervous tissues. Thus No. 38, a Mongolian imbecile and the second in his family, is said to have come of a healthy stock, being born under normal conditions, but two months previous to his birth his mother was shipwrecked and nearly drowned; while in the remaining twenty-two cases some adverse adventitious factor, occurring either at birth or during infancy, was always present. A study of these adventitious factors reveals the following interesting facts:—

(a) Of the fifteen firstborn children giving a positive reaction, eleven are in Group (c), *i.e.*, in the series of cases in the ætiology of which syphilis would appear to be the essential factor.

(b) Of the seven positive cases, the amential condition of each of which was said to be due to difficult and protracted labour with instrumental delivery, six are seen to be in Group (c).

(c) Of the seventeen positive cases, in each of which the mental deficiency was attributed to a severe infantile illness, the syphilitic virus would appear to be the essential element in ten.

(B) The Ætiological Analysis of the Twenty Cases giving "Weakly Positive" Reactions.

23	±	±	...	...	...	...	±	...	...	...	±	...	...	...	...	...	±	...	...	...	...	±	...
24	±	...	...	...	...	...	...	...	...	...	...	±	±	...	...	...	...	...	±d	...	...	±	...
25	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	±	...	...
26	...	±	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
27		±	...	...	...	...	...	...	...	...	...	±	±	...	...	...	±	...	...	...	...	...	...
28	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
29	...	...	±	...	...	...	...	...	...	...	...	...	...	...	±*e*	...	...	...	...	...	...	...	...
30	...	...	...	...	...	...	...	±	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...
31	...	...	...	...	...	...	...	...	...	...	...	±	±	...	...	...	...	...	...	...	...	±	...
32	...	...	...	...	...	...		...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	±
33	...	...	...	...	...	...	...	...		...	...	...	...	...	...	...	...	...	...	±	...	±	...
34	...	...	...	...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	±
35	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
36	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
37	...	...	...	...	...	...	...	...	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...
38	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...	...	...	...
39	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...
40	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
41	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
42	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±

a = a cretin whose paternal cousin is also a cretin.

b = a premature birth.

c = a ten months' baby.

d = the fifteenth child and the second of twins.

e = a cretin whose mother and sister had exophthalmic goitre.

N.B.—The sera of all cases printed in italics were *negative* when "heated."

(A) That the virus is undoubtedly an *auxiliary* and *augmentary* factor in the ætiology of eleven cases—viz., in Nos. 1, *2*, 3, *6*, 11, *23*, 24, 25, 26, 28, *29*.

(B) That it probably is the *exciting* or *determinant* factor in six cases—viz., in Nos. 5, *9*, 10, 27, 35, *36*.

(c) That it appears to be the *essential* factor in twenty-five cases—viz., in Nos. *4*, 7, *8*, *12*, 13, 14, 15, 16, *17*, *18*, 19, *20*, *21*, 22, 30, 31, 32, 33, 34, 37, 38, *39*, 40, 41 and 42.

(D) That in no case is it the *only* ætiological factor, for even on analysing group (c) it will be seen:—

(*a*) That though in two cases (viz., *18* and 37) the syphilis appears to be wholly responsible for the amentia, it in reality has produced the mental defect by acting upon already degenerated germ plasm. Thus in No. 37 the boy's father was said to have died of phthisis; and No. *18*, a Mongolian idiot, was the son of aged parents, being the eleventh child.

(*b*) In all the other twenty-three cases, the syphilis appears to be associated with damaged nervous tissues. Thus No. 38, a Mongolian imbecile and the second in his family, is said to have come of a healthy stock, being born under normal conditions, but two months previous to his birth his mother was shipwrecked and nearly drowned; while in the remaining twenty-two cases some adverse adventitious factor, occurring either at birth or during infancy, was always present. A study of these adventitious factors reveals the following interesting facts:—

(a) Of the fifteen firstborn children giving a positive reaction, eleven are in Group (c), *i.e.*, in the series of cases in the ætiology of which syphilis would appear to be the essential factor.

(b) Of the seven positive cases, the amential condition of each of which was said to be due to difficult and protracted labour with instrumental delivery, six are seen to be in Group (c).

(c) Of the seventeen positive cases, in each of which the mental deficiency was attributed to a severe infantile illness, the syphilitic virus would appear to be the essential element in ten.

(B) The Ætiological Analysis of the Twenty Cases giving "Weakly Positive" Reactions.

23	±	±	...	...	...	...	±	...	...	...	±	...	...	...	...	...	±	...	...	...	...	±	...
24	±	...	...	...	...	...	...	...	...	...	...	±	±	...	...	...	...	...	±d	...	...	±	...
25	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	±	...	...
26	...	±	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
27		±	...	...	...	...	...	...	...	...	...	±	±	...	...	...	±	...	...	...	...	...	...
28	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
29	...	...	±	...	...	...	...	...	...	...	...	...	...	...	±e	...	...	...	...	...	...	...	...
30	...	...	...	...	...	...	...	±	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...
31	...	...	...	...	...	...	...	...	...	...	...	±	±	...	...	...	...	...	...	...	...	±	...
32	...	...	...	...	...	...		...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	±
33	...	...	...	...	...	...	...	...		...	...	...	...	...	...	...	...	...	...	±	...	±	...
34	...	...	...	...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	±
35	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
36	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
37	...	...	...	...	...	...	...	...	±	...	...	...	...	...	...	...	...	...	...	...	...	...	...
38	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...	...	...	...
39	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...	...	...
40	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
41	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±	...
42	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	±

a = a cretin whose paternal cousin is also a cretin.

b = a premature birth.

c = a ten months' baby.

d = the fifteenth child and the second of twins.

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N.B.—The sera of all cases printed in italics were *negative* when "heated."

(A) That the virus is undoubtedly an *auxiliary* and *augmentary* factor in the ætiology of eleven cases—viz., in Nos. 1, *2*, 3, *6*, 11, *23*, 24, 25, 26, 28, *29*.

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(C) That it appears to be the *essential* factor in twenty-five cases—viz., in Nos. *4*, 7, *8*, *12*, 13, 14, 15, 16, *17*, *18*, 19, *20*, *21*, 22, 30, 31, 32, 33, 34, 37, 38, *39*, 40, 41 and 42.

(D) That in no case is it the *only* ætiological factor, for even on analysing group (C) it will be seen:—

(*a*) That though in two cases (viz., *18* and 37) the syphilis appears to be wholly responsible for the amentia, it in reality has produced the mental defect by acting upon already degenerated germ plasm. Thus in No. 37 the boy's father was said to have died of phthisis; and No. *18*, a Mongolian idiot, was the son of aged parents, being the eleventh child.

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(a) Of the fifteen firstborn children giving a positive reaction, eleven are in Group (C), *i.e.*, in the series of cases in the ætiology of which syphilis would appear to be the essential factor.

(b) Of the seven positive cases, the amential condition of each of which was said to be due to difficult and protracted labour with instrumental delivery, six are seen to be in Group (C).

(c) Of the seventeen positive cases, in each of which the mental deficiency was attributed to a severe infantile illness, the syphilitic virus would appear to be the essential element in ten.

(d) While of the five positive cases in which infantile head injuries were cited as the cause of amentia, the essential ætiological factor in four would appear to be syphilis.

Obvious deductions, however, are disappointing, and, inasmuch as more than one of the above adverse adventitious factors of birth and infancy occur in many patients in Group (c) (as is shown in Table E), the obvious deductions should not be drawn, nor could they be accepted as true from the results already stated. Selecting, however, for a decisive examination only those cases in which, in addition to the syphilis, there occurred *one* other adverse adventitious factor of birth or infancy, the following tentative statements may, perhaps, be presented, viz.:—

(a) That in three cases (19, *20*, and 39), though the amentia was said to be due to the strain and stress of primogeniture, the mental deficiency was probably primarily and essentially the result of syphilis and not of the parturition.

(b) That syphilis was probably also the primary and essential factor in the two cases (*21* and 22) in each of which the mental deficiency was directly attributed to difficult and protracted labour with instrumental delivery.

(c) That in two cases (40 and 41), perhaps also in three others (16, *17* and 31) where amentia was said to be produced by a severe infantile illness, syphilis and not the suggested illness was probably the cause of the mental defect. (The illness recorded in the histories of Nos. 31 and 41 was "infantile convulsions"; while in the other three it was due to the onset of "epilepsy," a disease from which they still suffer.)

(d) That in No. 42, in whom the mental defect was said to have appeared from the date of a head injury received in infancy, the essential cause of his amentia was probably not the injury but the syphilis, which, perhaps, was also the probable ætiological factor in No. *12*, another alleged case of infantile traumatic amentia.

In conclusion, then, it should again be noted and perhaps emphasised that in none of these forty-two cases giving a positive compluetic reaction did the syphilitic virus acting alone appear to produce the amentia. In every instance it would seem that the virus was associated with and acted upon inherently defective, diseased and degenerated, or damaged nervous tissues. And this, perhaps, is only to be expected, for, as will be recollected, the children of syphilitic parents need not necessarily be aments, although, as is also known, a minority of congenital syphilitics, if untreated or ill-treated, is liable to become the victims of various nervous lesions under mental or physical strain and stress; and this is especially so—in fact, it may even be said to be only so—in those patients in whom the central nervous system is in some the least way defective. Given a healthy nervous system, congenital syphilis, as is proved by common medical experience, will not produce amentia. On the other hand, it is quite possible, and even reasonable, to suppose that given an exceedingly virulent neurotoxic type of syphilis *in utero* the healthiest nervous system would be likely to fall a victim to the virus. Between these two extremes, the various grades of syphilitic amentia may be found.

(6) *Classification.*—Mr. Tredgold, in his book "Mental Deficiency," maintains that "there are two fundamentally different forms of amentia; there are also innumerable degrees; and it is convenient to describe certain distinctive clinical varieties." The forms of amentia Mr. Tredgold has called primary and secondary; the degrees are now jumbled together into four groups by Act of Parliament; the clinical varieties are well known. In the following paragraphs the lines of classification suggested by Mr. Tredgold will be followed with slight modifications:—

(*a*) The forms of amentia: Of the 100 cases serologically examined, seventy-six were cases of primary amentia and twenty-four cases of secondary amentia. Of the forty-two cases giving a positive compluetic reaction, thirty-two were cases of primary amentia, ten cases of secondary amentia, so that of all the cases

of primary amentia examined, a little over 42 per cent. were positive, and of all the cases of secondary amentia examined, nearly 42 per cent. were positive.

Moreover, as to the intensity of reaction in each group, nine of thirty-two cases of primary amentia gave "definitely positive" reactions, thirteen "weakly positive" reactions, and ten "doubtfully positive" reactions; while three of the cases of secondary amentia gave "definitely positive" reactions, three "weakly positive" reactions, and the remaining four "doubtfully positive" reactions.

(*b*) The degrees of amentia: By Act of Parliament the "innumerable degrees" of amentia are now legally grouped as four —idiots, imbeciles, feeble-minded, and moral imbeciles. All the 100 patients examined were either idiots or imbeciles. As a matter of fact, seventy of them may be considered to be imbeciles and thirty are idiots. Half of these thirty idiots gave positive reactions, in five the reaction being "definitely positive," in five "weakly positive," and in five "doubtfully positive"; while of the seventy imbeciles, twenty-seven gave a positive reaction, and of these seven were "definitely positive," eleven "weakly positive," and nine "doubtfully positive."

(*c*) The clinical varieties of amentia: No distinctive clinical type of syphilitic amentia has been described. Of the known clinical varieties the following occurred among the 100 cases examined:—

(I) Primary Amentia.

(1) Microcephalus	*Nil.*
(2) Mongolianism	11 cases.
(3) Simple amentia	65 cases.

(Ia) Primary Amentia with Complications.

(1) With paralysis only	2 cases.
(One mongol and one simple primary ament.)	
(2) With convulsions only	26 cases.
(All simple primary aments.)	
(3) With paralysis and convulsions	*Nil.*

(II) SECONDARY AMENTIA.

(1) Hydrocephalus	3 cases.
(2) Hypertrophicism...	1 case.
(3) Cretinism	4 cases.
(4) Simple amentia	16 cases.

(IIA) SECONDARY AMENTIA WITH COMPLICATIONS.

(1) With paralysis only	*Nil.*
(2) With convulsions only	10 cases.

(One hydrocephalic, one hypertrophic, and eight simple secondary aments.)

(3) With paralysis and convulsions	5 cases.

(One cretin, two hydrocephalic, and two simple secondary aments.)

Each of these varieties will now be considered (*vide* also Table F).

(1) *Microcephalus.*—Unfortunately no case was examined.

(2) *Mongolianism.*—Of the eleven cases examined only three were positive. In other words, in over 72 per cent. of these cases the sera did not react to the test. Of the three Mongols giving a positive reaction two were doubtfully positive and the other was weakly positive. Brief records of the life-histories of these eleven Mongols are appended:—

The Negative Cases.

Case 1.—Idiot, aged 14. (1) Ancestral history, *nil.* (2) Parental history, *nil.* Father a farm labourer. (3) Personal history: The third of five children; birth normal; infancy and childhood healthy.

Case 2.—Idiot, aged 25. (1) *Nil.* (2) *Nil.* Father a labourer. (3) The seventh of seven; fright of shipwreck to mother when three months pregnant; an eight months' child; birth normal; infancy and childhood healthy.

Case 3.—Idiot, aged 20. (1) *Nil.* (2) Father somewhat dull; father and mother aged about 35 when patient was born; father a clerk. (3) The second of three; fall of mother at seventh month; birth normal; infancy and childhood healthy.

Case 4.—Imbecile, aged 26. (1) *Nil.* (2) Father died of nephritis; mother healthy. (3) The fifth of six; fall of mother

just before full term; birth normal; infancy and childhood healthy.

Case 5.—Imbecile, aged 20. (1) Paternal grandmother, aunt, and sister epileptic. (2) *Nil.* Father manager of brickfields. (3) The only child; birth normal; infancy and childhood healthy.

Case 6.—Imbecile, aged 18. (1) *Nil.* (2) *Nil.* Father an engineer fitter. (3) The fifth of eight; birth normal; infancy and childhood healthy.

Case 7.—Imbecile, aged 22. (1) *Nil.* (2) Mother always very delicate; father a policeman. (3) The eighth of nine; birth normal; infancy and childhood healthy; has right internal strabismus.

Case 8.—Imbecile, aged 23. (1) *Nil.* (2) *Nil.* Father a bank clerk. (3) The fourth of five; a seven and half months' child; birth normal; infancy and childhood moderately healthy.

The Positive Cases.

Case 9.—Imbecile, aged 21. (1) *Nil.* (2) *Nil.* (3) The second of four; fright of shipwreck and drowning to mother two months before his birth; birth normal; infancy and childhood healthy; C.R. weakly positive.

Case 10.—Imbecile, aged 17. (1) *Nil.* (2) *Nil.* Father a doctor. (3) The firstborn; birth normal; infancy and childhood healthy; C.R. doubtfully positive.

Case 11.—Imbecile, aged 27. (1) *Nil.* (2) *Nil.* Father a furniture remover (died from accident). (3) Eleventh of eleven; birth normal; infancy and childhood fairly healthy; C.R. doubtfully positive.

(3) *Hydrocephalus.*—Only three cases were examined, and one of these gave a doubtfully positive reaction. Their life-histories are briefly as follows:—

Case 1.—Imbecile, aged 15. (1) *Nil.* (2) *Nil.* Father a labourer. (3) The sixth of ten; protracted labour and instrumental delivery; left hemiplegia, Jacksonian epilepsy; C.R. doubtfully positive.

Case 2.—Imbecile, aged 27. (1) *Nil.* (2) Mother died of erysipelas; father a doctor. (3) The second of seven; birth normal; infantile convulsions; C.R. negative.

Case 3.—Imbecile, aged 40. (1) *Nil.* (2) Father died of phthisis; mother died of "cancer"; father a schoolmaster. (3) The eighth of ten; worry to mother during pregnancy; birth normal; epilepsy when young; has left internal strabismus; C.R. negative.

(4) *Hypertrophicism.*—One case was examined, giving a definitely positive reaction. This boy is aged 13, and the fourth child in a family of four. When he was born his father was aged 70 and his mother aged 40. No consanguinity existed between his parents; no phthisis, alcoholism, or insanity was said to be present in the life-histories. His father died of general peritonitis; his mother is alive and healthy. Instrumental delivery was necessary at his birth, but with the exception of recurrent convulsive attacks from which he at present suffers, he has always been in good health. Mentally, he is an imbecile of a cheerful temperament and a happy disposition.

(5) *Cretinism.*— Four cretins were examined, and of these two gave positive reactions, one being definitely positive and the other doubtfully positive.

Case 1 (giving a definitely positive reaction).—A boy, aged 16, and the second of a family of six, all of whom are said to be normal. A paternal cousin is a cretin; the mother is said to be "neurotic"; otherwise the life-histories are normal. Both his parents are healthy, his father being a fisherman. The mother attributes the patient's condition to the fright she sustained on seeing the cretin cousin for the first time while pregnant with the patient. His birth was normal. He has taken extracts of the thyroid gland since the age of 18 months. He was operated on as a child for cerebral abscess. At the present day he is a strong, healthy, robust boy. He suffers occasionally from epistaxis, and recently he had two attacks of melæna. Mentally he is imbecile.

Case 2 (giving a doubtfully positive reaction).—A boy, aged 16, and the second of a family of three. No defect is recorded as present in his ancestral history. Both his parents are "neurotic," but physically in good health. His father is a warehouseman. His mother and her eldest child, his sister, have had exophthalmic goitre. The birth of the patient was normal. He has had thyroid from an early age. He is and has always been in good health. Mentally he is imbecile.

Case 3 (giving a negative reaction).—An idiot, aged 16, with a history of "neurotic heredity." His father, a parson, died of "heart disease"; his mother is alive and healthy. He is the only child, and instrumental delivery was necessary at his birth. He has had thyroid from an early age. He is epileptic. He also has a left otorrhœa, a right ptosis, and undescended testes.

Case 4 (giving a negative reaction).—An imbecile, aged 22, and the second in a family of five. Recorded in his family history is the fact that a maternal niece is feeble-minded and subject to epilepsy. His father died of "cancer of the kidneys." His mother is in good health, but she says she was unable to speak distinctly till the age of 12. His eldest sister is a cretin. His birth was normal, but his "mother used to think a great deal about a cretin when carrying him." No infantile injury or other illness is recorded. He has had thyroid from the age of 2, and is to-day robust, strong, and in good health. He is very deaf.

(6) *Simple Amentia.*—In the book aforementioned, Mr. Tredgold writes: "The majority of persons suffering from primary amentia present no special distinguishing features other than the anatomical and physiological anomalies common to aments in general; they may, therefore, be termed simple aments, and they correspond to the 'genetous' group of Ireland." "This term," he adds in a note, "is open to the objection that all primary aments may in reality be called 'genetous.'" In this paper both the "genetous" group of Ireland and the "simple aments" of Mr. Tredgold are called by the more exact name of "simple primary amentia." It is here suggested that the term "simple

TABLE F.—SHOWING THE RELATION OF THE REACTION TO THE CLINICAL VARIETIES OF AMENTIA EXAMINED.

Clinical variety.	Number of cases.	Number of "definitely positive" reactions.	Number of "weakly positive" reactions.	Number of "doubtfully positive" reactions.	Number of "negative" reactions.
(A) *Primary amentia:*—					
(1) Microcephalus	—	—	—	—	—
(2) Mongolianism	11	—	1	2	8 (72 %)
(3) Simple amentia	65	10 (15·3 %)	11 (17 %)	8 (12·3 %)	36 (55·4 %)
(B) *Secondary amentia:*—					
(1) Hydrocephalus	3	—	—	1	2
(2) Hypertrophism	1	1	—	—	—
(3) Cretinism	4	1	—	1	2
(4) Simple amentia ...	16	—	5	1	10
(C) *Amentia with complications:*—					
(1) Amentia with paralysis	7	—	—	2	5
(2) Amentia with convulsions	41	5 (12·2 %	9 (22 %)	7 (17 %)	20 (48·8 %)

amentia" should include a larger number of cases than those concerned in Mr. Tredgold's definition; that so it should be capable of division into two classes, corresponding to the two forms of amentia, and that these two classes of simple amentia should be termed "simple primary amentia" and "simple secondary amentia" respectively. Mr. Tredgold's definition, in fact, may be adapted as follows: Persons suffering from simple amentia present no special distinguishing features other than the anatomical and physiological anomalies common to aments in general; they may be divided into two classes corresponding to the two forms of amentia, and may be termed "simple primary aments" and "simple secondary aments" respectively. By simple primary amentia would be understood the "simple amentia" described by Mr. Tredgold, while simple secondary amentia would constitute all those cases of secondary amentia in which the mental defect is due to gross cerebral lesions that are the results of toxic, inflammatory, or vascular causes, but the patients themselves are not distinguished by any of the special

characteristics peculiar to the clinical varieties of secondary amentia definitely known and described (viz., hydrocephalus, cretinism, etc.).

Each of these two groups of simple amentia will now be considered.

(*a*) Simple Primary Amentia.—Of the 100 cases examined, sixty-five were cases of simple primary amentia, and of these twenty-nine (or 44·6 per cent.) gave positive reactions. Moreover, of these sixty-five cases, twenty-seven were cases of amentia with complications, and thirty-eight were uncomplicated cases. Of the latter, fourteen (or 36·8 per cent.) gave positive reactions, while of the former fifteen (or 55·6 per cent.) gave positive reactions. Again, of the twenty-nine cases giving positive reactions, ten gave "definitely positive" reactions, eleven "weakly positive" reactions, and eight "doubtfully positive" reactions. Of all the "definitely positive" reactions, 40 per cent. were given by the complicated cases, and of all the "weakly positive" reactions 45 per cent. were given by the uncomplicated cases.

(*b*) Simple Secondary Amentia.—Sixteen of these cases were examined. Ætiologically, they may be classified as follows: Simple secondary amentia due to—(i) "infantile convulsions," seven cases; (ii) recurrent convulsions in early childhood, three cases; (iii) other illnesses in infancy, four cases; and (iv) head injuries in infancy, two cases. The first two of these groups will be considered in the section dealing with "amentia with convulsions." It may here be recollected that the ætiological group of simple secondary amentia due to "recurrent convulsions in early childhood" was known by the older writers as "eclampsic amentia." To-day Mr. Tredgold calls the same group of cases "epileptic amentia," distinguishing them from "amentia with epilepsy," where the convulsions are a complication and not the cause of the amentia. Both these terms, however, tend to confusion and are, therefore, not employed in this paper. Of the remaining two ætiological groups of simple secondary

amentia, the sera of the four cases due to "other illnesses in infancy" gave negative reactions, the illnesses recorded being "sunstroke," "meningitis," "illness at teething," and "mastoiditis." Both the cases due to head injuries in infancy gave positive reactions, one being doubtfully positive and the other weakly positive. In the ætiological Table E these two cases are shown as Nos. *12* and 42 respectively, and they are very probably cases in which the syphilitic virus and not the alleged injury is the primary and essential cause of the mental defect.

(7) *Amentia with Complications.*—Of the 100 cases examined forty-three were cases of amentia with complications. Of these forty-three cases twenty-one (or 48·8 per cent.) gave positive reactions, while of the fifty-seven uncomplicated cases twenty-one (or 36·8 per cent.) gave positive reactions; so that of all the positive reactions obtained half were given by the uncomplicated cases and half by the complicated cases. Again, of the seventy-six cases of primary amentia examined, twenty-eight (or 36·8 per cent.) were cases with complications, while fifteen of the twenty-four cases of secondary amentia (*i.e.*, 62·5 per cent.) were complicated cases. Of all the cases of primary amentia with complications, fifteen (or 53·5 per cent.) gave positive reactions, while of the uncomplicated cases of primary amentia seventeen (or 35·4 per cent.) gave positive reactions. Of all the cases of secondary amentia with complications six (or 40 per cent.) gave positive reactions, while of the uncomplicated cases of secondary amentia four (or 44·5 per cent.) gave positive reactions.

The cases of amentia with complications will now be considered under two heads: (*a*) Cases with paralysis; (*b*) Cases with convulsions.

(*a*) Amentia with Paralysis.—The physical condition of seven of the 100 patients was complicated with paralysis, the types of paralysis being as follows: Hemiplegia, three cases; strabismus, three cases; and ptosis, one case. Of these seven cases, two gave doubtfully positive reactions, both being hemiplegias and

cases of secondary amentia. One of these two, a hydrocephalic, is also subject to "Jacksonian epilepsy."

(*b*) Amentia with Convulsions.—At the present day seventeen of the 100 cases examined suffer from recurrent convulsive attacks commonly designated by the convenient group-name of "epilepsy." In addition to these, eleven others have suffered from similar attacks when younger, but are not so afflicted now; and twelve others are said to have had "infantile convulsions." Moreover, one other case is subject to "Jacksonian epilepsy." In all, then, forty-one of the 100 cases examined have had convulsive attacks at some period of their lives. These cases are analysed in Table G.

TABLE G.—BEING AN ANALYSIS OF THE FORTY-ONE CASES OF AMENTIA WITH CONVULSIONS.

Clinical variety.	Number of cases.	Number of "definitely positive" reactions.	Number of "weakly positive" reactions.	Number of "doubtfully positive" reactions.	Number of "negative" reactions.
Recurrent convulsions at present day :—					
(1) Simple primary aments	15	2 (13 %)	4 (27 %)	3 (20 %)	6 (40 %)
(2) Hypertrophic	1	1	—	—	—
(3) Cretin (with paralysis)...	1	—	—	—	1
Recurrent convulsions in childhood :—					
(1) Simple primary aments	7	2	1	2	2
(2) Hydrocephalic (with paralysis)	1	—	—	—	1
(3) Simple secondary aments	2	—	—	1	1
(4) Simple secondary aments (with paralysis) ...	1	—	—	—	1
"*Infantile convulsions*" :—					
(1) Simple primary aments	4	—	1	—	3
(2) Hydrocephalic	1	—	—	—	1
(3) Simple secondary aments	6	—	3	—	3
(4) Simple secondary aments (with paralysis) ..	1	—	—	—	1
"*Jacksonian epilepsy*" :—					
(1) Hydrocephalic (with paralysis)	1	—	—	1	—

From this table it will be seen:—

(i) That, excluding the "Jacksonian epileptic," of the forty remaining cases of amentia with convulsions, twenty (*i.e.*, 50 per cent.) gave positive reactions, five being "definitely positive," nine "weakly positive," and six "doubtfully positive."

(ii) That excluding also the cases of "infantile convulsions" there are twenty-eight patients who are or have been subject to recurrent convulsive attacks. Of these, sixteen (a little over 57 per cent.) gave positive reactions, five being "definitely positive," five "weakly positive," and six "doubtfully positive."

(iii) That of the seventeen cases suffering at the present day from recurring convulsive attacks, commonly designated by the group-name of "epilepsy," ten, or nearly 59 per cent., gave positive reactions; and of these positive reactions 30 per cent. were "definitely positive."

Hence it would seem from the above study that of all the patients who have had convulsive attacks at some period of their lives, over 50 per cent. gave positive reactions; while of those who might have been designated "epileptic" at some period of their lives, a little over 57 per cent. gave positive reactions; and of those diagnosed as "epileptic" to-day, nearly 59 per cent. gave positive reactions.

Again comparing the figures given in Table G with the total number of cases giving positive reactions (viz., forty-two cases), it will be seen that of all the patients giving positive reactions twenty-one (or 50 per cent.) have had convulsive attacks at some period of their lives; sixteen (or 38 per cent.) might have been designated "epileptic" at some period of their lives; and ten (or nearly 24 per cent.) are diagnosed as "epileptic" to-day.

Considering now the non-convulsive cases, it will be remembered that fifty-nine of the 100 cases examined have never had a convulsive attack of any kind at any period of their lives. Of these fifty-nine cases twenty-one gave positive reactions. In other words, half the total number of positive reactions in this

series occurred in non-convulsive cases, and the other half in those who have had convulsive attacks at some period of their lives. To be more exact, 50 per cent. of the positive reactions occurred in non-"epileptic" cases and 38 per cent. in those cases which might have been designated "epileptic" at some period of their lives. On the other hand, as already noted, a little over 57 per cent. of these "epileptic" cases gave positive reactions, while of the non-"epileptic" cases only 35·5 per cent. gave positive reactions.

Other facts to be noted are as follows:—

(*a*) Seventy-six cases of primary amentia were examined, and of these twenty-six were cases with convulsions. Of the convulsive cases, fifteen (or 57·7 per cent.) gave positive reactions, while of the fifty non-convulsive cases seventeen (or 34 per cent.) gave positive reactions.

(*b*) Fifteen of the twenty-four cases of secondary amentia were cases with convulsions. Of these convulsive cases six (or 40 per cent.) gave positive reactions, while of the non-convulsive cases four (or 44·5 per cent.) gave positive reactions. Moreover, of the fifteen convulsive cases ten were cases with convulsions only, and of these five (or 50 per cent.) gave positive reactions.

(*c*) Eighty-one cases of simple amentia were examined, and of these thirty-six were cases with convulsions. Of the convulsive cases nineteen (or 52·7 per cent.) gave positive reactions, while of the forty-five non-convulsive cases sixteen (or 35·5 per cent.) gave positive reactions. Moreover, thirty-four of these cases were cases with convulsions only, and nineteen (or 55·8 per cent.) gave positive reactions.

Again, of the thirty-six cases of simple amentia with convulsions, twenty-six were cases of primary amentia and ten of secondary amentia. Of the twenty-six cases of simple primary amentia with convulsions, fifteen (or 57·6 per cent.) gave positive reactions, while of the non-convulsive cases of this type fourteen (or 35·8 per cent.) gave positive reactions. Of the ten

cases of simple secondary amentia with convulsions, four (or 40 per cent.) gave positive reactions; of the eight cases of this type with convulsions only, four (or 50 per cent.) gave positive reactions; while of the non-convulsive cases two (or 33·3 per cent.) gave positive reactions.

The last point to be investigated was the relation of the intensity of the "epilepsy" and the frequency of the convulsive attacks to the incidence and intensity of the reaction. Unfortunately no such relations were obtained. Three of the "negative" cases, for instance, were the severest cases of "epilepsy" examined; while of the "positive" cases the most severe and the mildest gave "definitely positive" reactions, the serum of the second worst was only "weakly positive," and so on. One slight feature of this series of cases, however, should be noted. It was found that the convulsive attacks in the "positive" cases tend to be far more frequent during the night and the early hours of the morning than they are during the day, while in the "negative" cases they are most frequent during the day. The intensity of the convulsive attacks in each instance appears to be characterised also in the same way. This feature of the "positive" cases, therefore, tends to bring them into line with other syphilitic conditions—*e.g.*, the syphilitic headache, which is said to be most intense towards the early hours of the morning.

Recapitulation.

The main points of this paper may be recapitulated as follows:

(1) *The Incidence of the Compluetic Reaction in the Cases of Amentia Examined.*—The blood sera of 100 aments were examined, and a "positive" reaction was found to be present in forty-two; but only twelve of these are to be regarded as "truly positive."

(2) *The Intensity of the Reaction in the Cases of Amentia Examined.*

(i) Sera were tested heated and unheated. Sera in which no hæmolysis occurred were recorded as "definitely positive"; those

in which partial hæmolysis occurred as "weakly positive." Sera in which the results differed when heated and unheated were recorded as "doubtfully positive." Of the forty-two sera giving a positive reaction, in twelve the reaction was found to be "definitely positive," in sixteen "weakly positive," and in fourteen "doubtfully positive"; but only the twelve "definitely positive" reactions are to be regarded as "truly positive."

(ii) Quantitatively, even the "definitely positive" reactions are to be considered as feeble reactions, for the syphilitic reagin present in each of these cases was invariably found to be in small quantities, being always enough to utilise two minimal doses of complement.

(3) *The Relation of the Presence of the Reaction to the Sex of the Patients Examined.*—This was not determined, as all the aments examined were males.

(4) *The Relation of the Presence of the Reaction to the Age of the Patients Examined.*—The reaction was found to vary with age. As a rule, it tended to diminish in incidence and intensity as the ages of the patients increased. It appeared, however, to be strongest and most frequent in patients between 16 and 21 years of age; and it tended to be more frequent and stronger in those below 16 than in those above 21 years of age. In considering the total percentage of the positive results obtained, it should be remembered that the majority of the patients examined were boys, 38 per cent. being between 16 and 21, and 57 per cent. under 21 years of age.

(5) *The Relation of the Reaction to the Forms of Amentia Examined.*—The reaction was obtained in a little over 42 per cent. of the cases of primary amentia, and in nearly 42 per cent. of the cases of secondary amentia. It tended to be a little stronger in the latter group of cases.

(6) *The Relation of the Reaction to the Degrees of Amentia Examined.*—Only idiots and imbeciles were examined. The reaction appeared to be more frequent and stronger in the idiots

than in the imbeciles; thus, 50 per cent. of the idiots examined gave a positive reaction, and in 16·6 per cent. the reaction was found to be "definitely positive," whereas it was present in 38·5 per cent. of the imbeciles, being "definitely positive" in 10 per cent.

(7) *The Relation of the Reaction to the Clinical Varieties of Amentia Examined.*

(i) In over 72 per cent. of mongols the serum did not react to the test. Of the eleven cases examined, a positive reaction was obtained in three, being "weakly positive" in one and "doubtfully positive" in the other two.

(ii) One of three cases of hydrocephalus gave a "doubtfully positive" reaction.

(iii) Only one case of hypertrophicism was examined, and this was found to be "definitely positive."

(iv) A positive reaction was obtained in two of four cretins, being "definitely positive" in one, and "doubtfully positive" in the other.

(v) Eighty-one cases of simple amentia were examined, and the reaction was found to be "definitely positive" in ten, "weakly positive" in sixteen, and "doubtfully positive" in nine. Excluding the "doubtfully positive" cases the reaction was found to be present in 32 per cent. of simple aments. It appeared to be more frequent in the cases of simple primary amentia than in the cases of simple secondary amentia.

(vi) Of the seven cases of amentia with paralysis, two, both hemiplegias, gave "doubtfully positive" reactions.

(vii) Excluding the "doubtfully positive" cases, the reaction was present in 41·2 per cent. of patients suffering at the present day from recurring convulsive attacks, commonly designated by the group-name of "epilepsy"; in 35·7 per cent. of those diagnosed as "epileptic" at some period of their lives; and in 23·7 per cent. of non-"epileptic" cases. It should also be

noted that of the simple primary aments with recurrent convulsions to-day, a "definitely positive" reaction was obtained in only 13 per cent.

(8) *The Rôle of Syphilis in the Ætiology of the Cases of Amentia Examined.*—Three points are to be noted:—

(i) That as the compluetic reaction is an index of existing syphilis, all the positive cases are to be regarded as weak syphilitic infections.

(ii) That these weak infections were intra-uterine or "congenital" in origin.

(iii) That the syphilitic virus did not appear to be wholly responsible for the amentia in each of these cases, but seemed rather to have been associated with and to have acted upon inherently defective, diseased and degenerated, or damaged tissues.

In conclusion, I should like to state how very grateful I am to Sir George Savage for his kindly interest in and generous appreciation of this my work, whereby it was submitted to the authoritative criticism of Major Mott, who, though he regretted that the technique employed was not in strict conformity with that of the "original" test, yet agreed the results obtained were of sufficient value to be placed before this meeting.

APPENDIX.

Showing some of the results published.

Names of observers.	Number of cases examined.	Number of "positive" results obtained.	Percentage of "positive" results obtained.
In France.			
Raviart, Breton, &c [1] ...	246	76	30·8
In Denmark.			
(*a*) Lippmann [2] ...	78	7	8·9
(*b*) *Idem*	(?)	(?)	13·2
In Germany.			
Kellner, Clemenz, &c. [3]	216	8	3·7
Dean [4]	330	51	15·4
Thomsen, Boas, &c. [5] ...	2,061	31	1·5
Kröber [6]	262	56	21·3
In America.			
Atwood [7]	204	30	14·6
W. C. Stoner and E. L. Keiser [8]	1,050	83	7·9
Dawson [9]	—	—	4·0
(*a*) Stevens [10]	21	2	9·5
(*b*) *Idem*	18	6	33·3
In England—			
Muirhead [11]	5	0	0
Schölberg & Goodall [12]	46	15	32·6
Chislett [13]	22	11	50·0
Gordon [14]	400	66	16·5
Fraser and Watson [15] ...	205	123	60·0
(*a*) Rees Thomas [16] ...	163	8	4·9
(*b*) *Idem*	—	—	10·0
Robertson & Findlay [17]	15	(?) 9	59·0
F. E. Batten [18] ...	2	0	0
(*a*) Mott [19]	257	21	8·1
(*b*) *Idem*	200	24	12·0
H. F. Stephens	100	12	12·0

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THE EXPERIMENTAL PRODUCTION OF TUBERCULOUS PERITONITIS IN GUINEA PIGS PREVIOUSLY EXPOSED TO X-RAYS.

By

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In some instances tuberculous infection gives rise to a clinical picture which is striking and typical—almost pathognomic; on the other hand, tuberculous disease, especially of certain organs, presents many difficulties of diagnosis; symptoms and signs are often latent and notably uncertain, and perhaps do not make themselves manifest until the disease is well established or the immediate demonstration of the tubercle bacillus by microscopical examination is a matter of great difficulty or even impossibility.

In view of the difficulties arising from the latter type of case, laboratory research has been invoked to evolve a method of establishing a certain diagnosis in the early stages of infection. Obviously the most certain method must depend upon the demonstration of the presence of the specific infecting agent, viz., the turbercle bacillus. In doubtful cases the most reliable precedure is the inoculation of the suspected material into a susceptible animal, *e.g.*, the guinea-pig.

PART I.

Methods of Diagnosis of Tubercular Disease.

(A.) Direct microscopical examination.
  1. Antiformin method (of Uhlenhuth).
  2. Centrifugal method (of Crabtree).

(B.) Cultural methods.

(C.) Inoculation methods.
  1. Ordinary inoculation methods.
    (a) Subcutaneous.
    (b) Intraperitoneal.
  2. Rapid inoculation methods.
    (a) Inoculation of suckling guinea-pigs.
    (b) Intra-ocular.
    (c) Inoculation after exposure to X-rays.

(D.) Demonstration of specific hypersensibility (cutaneous reaction).

(E.) Demonstration of specific antibodies (opsonic index).

(A.) Direct microscopical examination of the materies morbi, when a positive result is obtained, and the tubercle bacillus is found, may be regarded as the most rapid method of establishing a diagnosis of tuberculosis. The demonstration of the bacillus is, however, one of the chief difficulties we have to contend with in looking for a tubercular cause in any given infection. In examining pathological material obtained from various sources, one finds a great divergence in the number of tubercle bacilli found; some specimens, for example, sputum, may be crowded with the bacilli, while in others repeated and prolonged examination may fail to discover their presence owing, firstly, to difficulty in staining the tubercle bacillus, and, secondly, to the fact that in certain materials, viz., urine, cerebrospinal fluid, pleural effusions, pus from an empyema, and scrapings from tuberculous glands, fæces, etc., owing to the dilution they undergo, the bacilli are present relatively in very small numbers indeed.

With regard to the difficulty in staining, tubercle bacilli stain indifferently with ordinary watery solutions of dyes, prolonged treatment with, or warming the solution being required. The best stain to employ consists of one part of saturated alcoholic (95 per cent.) solution fuchsin and nine parts of 5 per cent carbolic acid. Many new stains have been introduced, but none have stood the test of time like this. A factor which at the present time increases the difficulty of staining is the unreliability of the fuchsin now available. As some hold that not one half of the tubercle bacilli in a preparation are stained when it is examined, the reason for failure in demonstrating them in specimens where they exist in small numbers (urine, cerebrospinal fluid, etc.) will become apparent, and the great value of overstaining will readily be seen. In routine work much time is saved by using the cold method. This consists in immersing the preparation in the cold stain for twenty-four hours.

Another factor which operates in increasing the difficulties of identifying the tubercle bacillus in stained preparations is, that its staining properties, and morphological appearances are common to other acid fast bacilli, *e.g.*, bacillus smegma, bacillus butyricus, etc., and it is often impossible by microscopical examination to differentiate between these latter bacilli and the tubercle bacilli.

The antiformin method of demonstrating the tubercle bacillus in sputum, fæces, etc., was introduced by Uhlenhuth in 1908, for the detection of the bacilli in material where they exist only in small numbers. Antiformin consists of equal parts of liquor sodæ chlorinatæ and 15 per cent. aqueous solution of sodium hydrate. The method of using antiformin is as follows:—an equal amount of antiformin is added to the suspected material and the mixture thoroughly shaken up. (A solution which does not foam well at this stage is useless.) It is then placed in an incubator at 37°C. for half an hour, during which period it is shaken occasionally. The material, now thoroughly digested, is centrifuged at high speed for a few minutes, after which the super-

natant fluid is poured off. The centrifuge tube is then filled up with saline and the sediment is well shaken and again centrifuged. The saline is then poured off and the last step is again repeated by adding fresh saline and again centrifuging; the saline is poured off and the sediment remaining may now be filmed, stained and examined microscopically. Antiformin rapidly destroys most bacteria, but tubercle bacilli and other acid fast bacilli appear to be able to resist its action for considerable periods, and hence in a specimen crowded with pyogenic organisms, one is able to dissociate the tubercle bacilli and concentrate them in the sediment obtained after the final centrifuging of the material.

I have employed this method for two distinct purposes : (1) For concentration of the bacilli in the specimen as a preliminary before staining. (2) For removing organisms other than the tubercle bacilli prior to inoculating the material into experimental guinea-pigs.

I do not consider the method of much more value than direct microscopical examination for detecting tubercle bacilli in the specimen, as it was my experience that where I failed to find tubercle bacilli by direct examination of the specimen, I was not often successful in demonstrating them by the antiformin method.

The outstanding advantage of the method, to my mind, is its capacity for destroying ordinary pyogenic organisms without exerting any great lethal influence on tubercle bacilli. This characteristic is decidedly advantageous when one wishes to make an animal inoculation intraperitoneally, as it minimises the risk to the animal of rapid death from acute peritonitis due to the common pyogenic bacteria.

In specimens treated with antiformin, the tubercle bacilli appear to retain their virulence for some time. Two specimens used by me for inoculation (one sputum, and the other fæces) were left in the cold room for ten days after antiformin treat-

ment, and the subsequent post-mortem on the animals inoculated with these materials showed plentiful tubercular lesions.

Centrifugal Method of Crabtree.—Crabtree devised a method for demonstrating tubercle bacilli in urine. One of the difficulties of demonstrating the tubercle bacilli in urine is the fact that the bacilli are of the same density as the urine itself, and only bacilli entangled in shreds of mucus get precipitated by the centrifuge. He took advantage of the difference in density between the bacilli and pus, to concentrate the bacilli in a large amount of urine (having got rid of the pus by slowly centrifuging the specimen for a few minutes) into a small sediment and by mounting the sediment in cover glass preparations; he found the bacilli in large numbers. He mentions as dangers of erroneous diagnosis by this method—

(1) Presence of other acid fast bacilli.

(2) Presence of tubercle bacilli left over in the centrifuge tube from examination of another specimen.

Crabtree claims satisfactory results with this method. It is apparently a simple procedure which does not require very elaborate apparatus, beyond a high speed centrifuge. It is not, however, an absolute proof of the absence of tubercular disease if the bacilli are not found in the urine. Tubercle bacilli are numerous in tuberculous disease of the kidney, especially of the pelvis; but in tuberculous affections of the bladder the bacilli may be few in number, and in these cases the centrifuge may fail to establish their presence.

Cultural Methods.—The most recent contribution to our knowledge of the cultivation of the tubercle bacillus has been made by Petroff. His method has been confirmed and modified by various workers. Keilty adopted this method, and I give here his experiments to demonstrate the presence of the tubercle bacillus in sputum, where negative results have been obtained by other means.

The *modus operandi* is as follows:—

Five c.c. of sputum is collected in a sterile bottle and mixed with 3 per cent. sterile sodium hydroxide and incubated at 37°C. for thirty minutes, during which time it is shaken frequently. A piece of sterile litmus is then placed in the bottle and the fluid is neutralised with sterile normal hydrochloric acid. It is then centrifugalised at high speed for ten minutes and the sediment is planted on three tubes of special medium. The medium consists of gentian violet, egg and veal. These tubes are incubated at between 38°C. and 39°C., the best results being obtained where an even temperature is maintained.

Excellent results appear to have been obtained with this method. Keilty reports having found the earliest evidence of growth as follows:—One tube showed a growth on the second day, and two on the fourth day, the average being fourteen to twenty-one days. Whitridge Williams and Ward Burdick, working with Petroff's medium, found that it became contaminated with spore bearing organisms which caused liquefaction of the medium, and consequent destruction of hopeful cultures. They, therefore, modified the medium and employed egg white solution, egg yolk solution, meat infusion, and powdered agar; these were mixed and sterilised in an autoclave for fifteen minutes and then 1 per cent. gentian violet was added (alcoholic solution). The sputum was prepared as in Petroff's method, and positive results were obtained in from 14 to 21 days. This method of diagnosis even when positive results are obtained cannot be regarded as other than slow.

Inoculation Methods.—The earliest inoculation experiments with tubercular material were made by Marcet in 1867, and in in the following year by Klebs. Marcet decided to experiment with guinea-pigs, and took as his starting point the results obtained by Villemain who practised inoculation of tubercular material into rabbits. The inoculation was made by passing a needle with a thread (which was saturated with sputum from the suspected case) through the skin, and by pressing on the thread on with-

drawal the matter it contained was deposited in the subcutaneous tissues where it remained. The site of inoculation was the groin external to the genital organs on either side. The experiments showed positive results in from 43 to 56 days. The tubercular lesions in the inoculated animals were found variously in the spleen, liver, mesenteric glands, lungs and cervical lymph glands. Microscopical examination showed small granular cells, large granulated cells, and pus cells. The affected parts were found to be soft and cheesy. It will be noted from the original communication that these experiments were done before the discovery of the tubercle bacillus by Koch; by this discovery and the subsequent proof of the causal relationship of the bacillus to tubercular disease, the value of Marcet's experiments in suspected cases was greatly enhanced.

Marcet at first worked largely with sputum and he maintained that a negative result after 53 days, by inoculation of sputum from a patient in what he described as the third stage of phthisis, was sufficient evidence of arrest of the disease, the patient being in a fair way to recovery. However, in his original paper he states that he had yet to show that the non-appearance of tuberculous lesions in the animals inoculated with expectoration from a supposed case of phthisis might be considered evidence of the patient not being tubercular. This he considered to be difficult.

This method of inoculation has been employed without fundamental change since Marcet's time, and although it is a certain method of diagnosing the disease when a positive result is obtained, it is associated with many disadvantages. Firstly, the delay caused in waiting for a positive result gives time for the progress of the tubercular disease in the patient, and so influences the prognosis and the subsequent hope of cure.

Secondly, if negative at the end of six weeks or even three months, it does not necessarily preclude the presence of tubercular disease. Thirdly, any prolonged observation period in experiments of this nature is to be deprecated owing to the risk that

the animal may contract the disease primarily, or from another source, or may fall a victim to some intercurrent infection.

Rapid Inoculation Methods.—Various workers have attempted to shorten the observation period. In 1903 L. Nattan Larrier and V. Griffon inoculated the suspected material into the breast of a suckling guinea-pig, the gland being susceptible to inoculation all the time during suckling and during the last days of gestation.

An animal was chosen which had recently borne her young. From 1 to 3 c.c. of the tubercular material was injected into the mammary gland, on the inner side of the nipple, any excess of the inoculated matter causing a reflux from the nipple.

After a few days the gland becomes hard and swollen, the lacteal secretion is modified, it becomes serous and yellow, and finally purulent. A diseased inguinal gland appears in two or three weeks and a tubercular mastitis develops which ulcerates and opens through the skin, and the animal dies with general tuberculosis. Films taken from the nipple each day revealed the presence of the tubercle bacilli in from a week to fifteen days. The bacilli were found in clumps or alone or enclosed in polymorphonuclear leucocytes.

The method appears to be a reliable one as far as it goes, but it will be obvious that the difficulty of securing suckling guinea-pigs just when needed is one which precludes the use of this method for practical purposes or as a routine procedure.

Intraocular Inoculation.—A comparatively rapid method of arriving at diagnosis of tuberculosis by animal inoculation is intraocular inoculation of rabbits. This method was practised by Valem in 1884. Any foreign body introduced into the eye will rapidly set up ophthalmia. The inoculation of tubercular material first apparently acts as a foreign body, but following the amelioration of the symptoms resulting from its mechanical action appears the specific lesion in the iris which is diagnostic of tubercular disease.

Valem gives a diary of the result of inoculation into both eyes of a rabbit :—

Third day.—Intense ophthalmia of both eyes; hypopyon; iritis and infection of the globe; complete blindness.

Eighth day.—A great amelioration of inflammatory symptoms produced spontaneously.

Tenth day.—Hypopyon which occupied two-thirds of the anterior chamber of both eyes nearly absorbed. The cornea of the left had recovered its transparency except inferiorly and at the level of the inoculation wound.

Twelfth day.—Limited point of vascularisation on the left iris.

Fifteenth day.—Two granulations appear on this point, which project clearly on the pupillary border.

Thirtieth day.—New granulations develop. Some appear on different points of the iris. The cornea at level of wound presents well circumscribed yellow projections on which two little white spot-like tubercles develop.

Fifty-fifth day.—Animal killed. Lungs scattered with tubercles; no other organs affected.

Tubercle bacilli are difficult to demonstrate in films taken from the lesions found in the affected eye.

By this method of intraocular inoculation a diagnosis of tuberculosis may be made in from fifteen to thirty days. The method may be fairly described as a comparatively rapid one.

Inoculation with the aid of Rontgen Rays.—The most recent attempt to abbreviate the observation period was introduced by Morton, of New York, in October, 1916. His experiments consisted of the inoculation of known and suspected tubercular material into the peritoneal cavity of a guinea-pig which had been recently exposed to X-rays.

The method employed by him was firstly to expose a guinea-pig to X-rays. In doing this, the animal was placed in a cardboard box, twelve inches from a Coolidge tube, and exposed to

the rays for ten minutes. A five milliampere current was used backing up eight and a half inches of spark between the points. The animals were inoculated either shortly before or after the X-ray exposure. Morton found that tubercular lesions were manifest in the animals in ten days (the earliest was seven days). In his publication he gives the results of twenty experiments, ten of which were from cases of known tuberculosis and another ten were from cases in which it was necessary to rule out a diagnosis of tuberculosis. Out of the whole series of twenty he obtained ten positive results (in from seven to fourteen days). Nine of these were from known tuberculosis specimens, and the remaining one was from a case in which it was necessary to eliminate the diagnosis of tubercular disease.

In his table of experiments he reports that two X-rayed animals died of streptococcal infection the day after inoculation. As I shall show later, this can be avoided by the use of antiformin in preparing the specimen for inoculation.

The microscopical picture of the lesions found in the X-rayed guinea-pics according to Morton showed coagulation necrosis and caseation, with a zone of endotheloid cells, no giant cells and a remarkable absence of small celled infiltration. There was no enclosing fibrous layer such as is found in slowly growing tubercles. This method seemed so full of promise that I proceeded to investigate it carefully My experiments are given in Part III. of this paper.

It will be noted that Morton worked only with urine for diagnosis in renal cases, but seeing the possibilities in many other directions I selected a miscellaneous collection of specimens and experimented on them more or less on the lines indicated above. When dealing with my own experiments I shall indicate the modifications introduced.

Demonstration of Specific Hypersensibility.—Tuberculin reactions.—Tuberculin for diagnostic purposes has been used in different ways. I will here only refer to methods which have come under my own observation.

(a) Koch's old tuberculin inoculated hypodermically, and used for diagnostic purposes only as a last resort, is not without its dangers and certainly not without its disadvantages. Its use is attended by danger in cases with extensive physical signs, heart disease, recent hæmoptysis, great dyspnœa, nephritis, epilepsy and recent acute diseases. In his book on tuberculin treatment Sahli refers to the risks attending tuberculin for diagnostic purposes, and he points out how illogical it is to expose patients to the danger of over-loading with toxin merely for diagnosis, after having emphasised the fact that tuberculin treatment is only harmless when the greatest care is taken with dosage and all reaction is avoided. To be of diagnostic value it is necessary to make a careful selection of cases; for example, cases with temperature of 100° F. are contra-indicated, and this necessarily rules out a large proportion, as many of the patients present themselves for examination with a pre-existing pyrexia. The question also arises of the specific value of tuberculin for diagnosis whatever method be employed. It is admitted that an old and cured tubercular lesion will give a reaction, and when it is remembered that 90 per cent. of persons at autopsy show evidence of healed tubercular lesions, it will be agreed that in adults, for a conclusive diagnosis of active tubercular trouble, it is of doubtful value.

(b) Von Pirquet's reaction has the merit of being a safe procedure; its diagnostic value in adults, however, is negatived by the fact that old and healed lesions readily react. It is said to be useful in cases not over four years of age.

(c) Calmette's ophthalmic reaction is said to be unreliable, and is attended with risk; personally, I have seen severe conjunctivitis follow its use, and when its limited application as an adjunct to diagnosis is considered, it makes one hesitate to experiment with such an important and delicate organ as the eye.

Demonstration of Specific Antibodies.—The specific antibodies which are searched for when the diagnosis of tuberculosis is made by serological methods are (1) agglutinins, (2) such

specific antibodies as are capable of fixing complement, (3) opsonins. Agglutinins are readily produced against tubercle bacilli and their products by repeated injections of these substances, and appear to some extent in the course of the disease. From the point of view of diagnosis, the test for opsonins is the most important and reliable provided a series of observations are carried out at short intervals, since chance samples of blood may fail to give any clear indication.

Complement fixing antibodies can frequently be demonstrated in the serum from a tuberculous patient, but the amount present is sometimes so small as to lead to a negative result in the test as ordinarily performed. The Bordet-Gengou reaction as applied to the diagnosis of tuberculous infection fails to attain the standard of reliability that we expect to attain from the same test as applied to the diagnosis of syphilitic infection.

Opsonins which aid in the phagocytosis of the tubercle bacillus can be demonstrated as specific antibodies; their function being to prepare the bacilli for ingestion by the leucocytes. Neither the opsonic index alone, nor the agglutination test, can be regarded as of absolute diagnostic value for tuberculosis, because normal agglutinins and opsonins which act on tubercle bacilli to a greater or less extent are present in healthy persons.

The demonstration of opsonins may be regarded rather as an index to the progress and course of the process of immunisation against tubercular infection, and especially is this the case in the treatment of the disease by vaccines or toxins of tuberculosis.

PART II.

The Effect of X-rays on the Blood.

Attention has been directed recently towards the role of the lymphocyte in tubercular processes. It has been observed that in rapidly fatal miliary tuberculosis the lymphocytes present in the peripheral blood fall often below 10 per cent. On the other hand, in cases with early tubercular infection or old healed lesions the lymphocytes form 50 per cent. of the total white cells. Further in rapidly developing miliary tuberculosis relatively few lymphocytes are found in the individual tubercles, while in the subacute forms the tubercles contain large numbers of lymphoid cells.

Heretofore a round-celled infiltration occurring about a slowly growing or healing cancer has been assigned, as in tuberculosis, a secondary role, the lymphoid elements being supposed to be due to the result of tissue disintegration. In tissue grafts it has been shown that the lymphocytes are the chief agents in causing destruction of the introduced tissue. Experiments on the chick embryo have also demonstrated this fact. The chick embryo normally is unable to resist the growth of implanted tissues from a foreign species; if, however, it is provided with a graft of adult chicken lymphoid tissue, it is well able to resist the growth of the implanted tissue.

If the lymphoid system of an adult animal be depleted, by exposure to X-rays, the animal loses its power of resistance to heterologous tissues and implanted tissues will grow readily in it.

Morton and Murphy, working on white mice in connection with transplantation of cancer, employed the X-rays in their experiments. They found that repeated small doses of X-rays destroyed the major portion of the lymphoid system without causing apparent injury to the other tissues or producing any effect detrimental to the health of the animal. In their reports

they state that after exposing the animals to the rays from a Coolidge tube the lymphocyte cells were much reduced in number. The series of experiments in this connection showed that the resistant state to transplanted cancer in white mice is accompanied by marked lymphocytosis, but that the tumours in the mice exposed to X-rays grew much more rapidly than in the animals untreated with X-rays. Heineke has also shown that the effect of the X-rays is first manifested by its destruction of the lymphocyte.

The effect of the X-rays on the guinea-pig's blood is very marked. The total number of leucocytes is often reduced by half, but the most remarkable feature is the great depression in the number of small lymphocytes. The normal differential count in the guinea-pig gives about 30 per cent. small lymphocytes, but after a single massive dose of the X-rays it can be demonstrated that the number may fall as low as 5 per cent. Morton found that the depression after the exposure to the rays lasted ten days, but carried his observations no further. I have made differential counts up to the end of fifteen days and found the lymphocyte count still depressed. The white cells themselves appeared to be normal in character, and I did not find in any of the many films examined any abnormal forms such as may be found in blood diseases. I did not follow the reaction in the blood cells beyond 15 days, as in my experiments this was the maximum duration of the observation period, and at this point the animals were killed for post-mortem examination. In this connection it might be interesting to observe the subsequent changes, if any, occurring in number and character, in the white cells during the progress towards the normal count.

In contrast to the differential count obtained in the guinea-pig after the X-ray exposure is the conduct of the leucocytes in an ordinary tuberculous infection in man. Here the leucocytes may be increased, decreased, or normal in the incipient stages, but as the disease progresses the leucocytes usually increase in number, and in advanced cases total white counts

of ten to twelve thousand or higher are not unusual. In low blood counts the small lymphocytes (in marked contrast to X-rayed animal blood) are increased in number.

Cases which present Difficulty in Diagnosis.

(a) Serous effusions are frequently obscure in their origin, and the question invariably arises as to whether they are tuberculous in origin.

Various methods have been employed to differentiate between the tuberculous and the non-tuberculous serous effusions, one of which is cytodiagnosis. By this method the diagnosis is made by a differential count of the cells found in the fluid. A large number of lymphocytes favours a diagnosis of tubercular disease of the affected membrane. However, not all fluids showing a preponderance of lymphocytes can be regarded as tubercular from the cellular formula alone, as long standing exudates and chronic passive congestion may show an excess of lymphocytes.

Tubercle bacilli are comparatively seldom found in peritoneal effusion by ordinary microscopical examination, and this comparative scarcity is also found in pleural effusion. It is believed to be due to the adhesion of the bacilli to the serous membrane. With a view to facilitate the detection of the bacilli in pleural and peritoneal effusion, Jousset designed a means for concentrating them in the fluid available for examination. His method briefly is as follows:—The fluid is allowed to clot and to it is added digestive material, *e.g.*, pepsin, glycerin, and strong hydrochloric acid, sodium fluoride, and distilled water. It is then placed in an incubator for thirty minutes and afterwards centrifuged, the resulting sediment being examined for tubercle bacilli.

Zebrowski also devised a method in which he prevented clotting of the fluid for examination by adding an equal volume of 10 per cent. sodium fluoride, the fluid was left standing for twenty-four hours, then centrifuged, and the sediment examined for the bacilli. Both claimed to be able to discover the

bacilli more easily by their respective methods, but the most reliable test for establishing a diagnosis of tubercular infection was found to be by inoculation of guinea-pigs.

Le Demaney used the guinea-pig for inoculating the suspected effusion. He also used large amounts of fluid which he injected at intervals, and he allowed his experiments to extend over three months. The delay in arriving at a diagnosis in this way is obviously a disadvantage. When one remembers that pleural effusions are more frequent at the onset of pulmonary tuberculosis than during its course, that cirrhosis of the liver has a decided tendency to become tubercular, and also that it may be difficult to avoid mistakes in diagnosis between hepatic cirrhosis and tubercular peritonitis, it will become apparent that an early diagnosis will be useful both in determining the line of treatment to be adopted and also in giving a prognosis, an infectious and a non-tubercular cause giving a greater hope of cure.

In this connection may be mentioned the difficulties obtaining in determining the nature of an empyema. Attempts at staining the pus for tubercle bacilli are usually without result. Previous inoculation methods were discounted by the fact that large amounts of the pus could not be inoculated into guinea-pigs without a rapidly fatal termination. This difficulty may now be overcome by the use of antiformin.

(b) *Early Phthisis.*—The diagnosis of early phthisis is attended by much difficulty, and even in expert hands many cases are met with in which, at the onset, it cannot be said that they are definitely tuberculous. Symptoms and physical signs are undoubtedly helpful, but often equivocal, and simulate other conditions, and until the presence of the tubercle bacilli in the sputum is detected the diagnosis may be in abeyance.

It has been found that the bacilli do not make their appearance in the sputum (in any case in sufficient numbers to be easily demonstrated by ordinary microscopical examination) until ulceration of the lung has occurred. Dettweiler maintained that

elastic fibres in the sputum were always accompanied by tubercle bacilli, but these might be so few in number as to escape detection. The inoculation of sputum into a guinea-pig will often reveal tubercle bacilli that cannot be found by repeated microscopical examination. Much time may, therefore, be lost before the tubercular nature of the disease is established, and the advantage of an early diagnosis cannot be over-rated.

(c) *Fæces.*—The detection of tubercle bacilli in fæces is not by any means an easy matter, and in my experience the ordinary method of examination leaves much to be desired. In the routine examination of specimens from the wards or out-patient department of a large hospital, negative rather than positive results are the rule. The low percentage of positive findings is not altogether accounted for by the selection of cases (that is, cases where the diagnosis of tuberculous disease is remote), but to some extent, anyhow, by the difficulty in successfully demonstrating the bacilli in the preparation.

These specimens are crowded with many other organisms. (This difficulty has been overcome to some degree by using the antiformin method before staining), but in addition to this the bacilli in tubercular diseases of the bowel or peritoneum are very few in number, and repeated and exhaustive examination of film preparations fails to lead to their discovery. Here, again, the only certain method of diagnosis is by inoculation, but as in tubercular disease of other sites the time element to some degree counteracts its advantages when the inoculation is made without the aid of the X-rays.

The finding of the tubercle bacillus in the fæces helps materially to establish the tuberculous element in such conditions as ulcerative enteritis, stenosing enteritis, chronic hyperplastic enteritis, and peritonitis with ascites in children. The finding of the bacilli is not an absolute criterion of the existence of tuberculous disease in the intestine, as when infected sputum is swallowed, tubercle bacilli may be found in the fæces, before an intestinal lesion has occurred, but their presence taken in

conjunction with other symptoms and signs is a valuable adjunct in the confirmation of a diagnosis of tubercular disease.

(d) *Urine.*—Churchman, speaking of renal tuberculosis at the New York Academy of Medicine laid emphasis on three points in diagnosis. Firstly, that renal tuberculosis may occur in a person who is otherwise apparently in perfect health. Secondly, renal symptoms are the exception and not the rule in renal tuberculosis. Thirdly, an impalpable kidney is no guide to the presence or absence of either enlargement of the kidney or of tubercular disease of the organ.

From these observations it will be seen that the diagnosis of renal tuberculosis may be easily overlooked from the clinical manifestations alone, but in addition to these factors there is also the difficulty attending the isolation of the bacillus from the urine.

Up to the present time the methods employed to demonstrate tubercle bacillus in urine have been by—

(1) Centrifugalizing at high speed.
(2) Animal inoculation.
(3) Cultural and other methods.

I have already dealt with these special methods, but I should here again emphasise Crabtree's observations on the great value of animal inoculation as the final test. The disadvantage of animal inoculation mentioned by him has, in my opinion, and experience, been overcome by Morton's use of guinea-pigs X-rayed previous to inoculation.

(e) *Meningitis.*—The micro-organisms which most frequently invade the meninges are those of tubercle, pneumonia, typhoid septicæmia, cerebrospinal fever, and its sporadic form of posterior basic meningitis. Tubercular meningitis is practically always a part of a more generalised infection. There is always some other focus of tubercular infection in one of the other organs, either lungs, glands, or some other part of the body.

Tubercular meningitis affects children more commonly than adults, and the clinical picture generally gives a clue to the diagnosis. The growth of the tubercle is accompanied by a serous exudate of varying intensity. The effects produced by the tubercular exudate may be summed up as (1) Irritation and compression of different parts of the brain. (2) General rise of intracranial pressure. (3) Local effects of the irritation and compression.

The diagnosis is usually arrived at by the clinical manifestation, and also by examination of the cerebrospinal fluid obtained from a lumbar puncture. Well-marked lymphocytosis is usually present, and in a very few cases the tubercle bacilli can be detected by staining with Zeil Neelsen method after centrifugalising the specimen. It is, however, very rare to find the tubercle baccilli in this way, and previous methods of diagnosis from the cerebrospinal fluid alone were dependent on the increase of lymphocytes in the fluid examined. The old method of inoculation of a guinea-pig is obviously out of the question as an aid to diagnosis, but the method of inoculation with X-rays may be of use where the case comes for diagnosis early in the course of the disease. I employed one specimen (a cerebrospinal fluid for a suspected case of tubercular meningitis) for inoculation into a guinea-pig with the aid of exposure to X-rays. Unfortunately the animal died within a few days from some unknown cause, and I was not able to find any evidence of tubercular growth in any of the organs; but the post-mortem on the patient confirmed the clinical diagnosis.

In any case the prognosis is not affected by an early diagnosis, as there is no evidence to show that a case of tuberculous meningitis is likely to recover. Furthermore, the meningeal inflammation is often only the more prominent part of a widely spread infection.

PART III.

Inquiries into the value of Morton's Method.

Seeing the possibilities of rapid diagnosis of tubercular disease in cases other than renal, I undertook to repeat Morton's work with a miscellaneous collection of specimens. The specimens were derived from the wards and Out-Patients' Department of Guy's Hospital, having been sent to the Bacteriological Laboratory for routine examination, and there I conducted all my experiments. The actual inoculations were performed for me either by the Director of the Department, Dr. Eyre, or the then Assistant Bacteriologist, Dr. Una Griffin.

The specimens which came under my observation, and with which I worked, were :—

(1) Sputum.

(2) Urine.

(3) Fæces.

(4) Effusion from the pleura.

(5) Cerebrospinal fluid.

The following is a resumé of the method I employed in dealing with the material for examination—

An ordinary film preparation was first made from the specimen to hand, and this was stained by the Zeil Neelsen method. I obtained excellent results with this stain by omitting the heating stage of the proceeding and leaving the preparation immersed in cold carbol fuschin for 16 to 24 hours. A larger number of bacilli appear to take up the stain when treated in this way than when stained by the original method.

If the film when examined for tubercle bacilli contained any pyogenic organisms, the specimen was subjected to treatment with antiformin before being inoculated.

Before inoculating any specimen without previous treatment with antiformin, it was first proved free from ordinary pyogenic organisms by being planted on culture media overnight. If these cultures proved to be negative, the antiformin was not used.

In my early experiments the tubercular material was inoculated into the guinea-pig just as received, without any preliminary treatment with antiformin, with the invariable result that the animals died within a day or two from an acute pyogenic infection—due to streptococcus, pneumococcus, or bacillus coli. In order, therefore, to minimise the risk of infection by any organisms other than that of tubercle bacillus, especially when dealing with specimens of sputum and fæces, I subsequently made it a routine procedure to subject the specimen to treatment with antiformin before inoculation. I found the antiformin method most useful for the purpose of obtaining a clean specimen free from the various pyogenic organisms, and it had the additional advantage of enabling me to concentrate the bacilli in the sediment obtained after centrifugalisation. In using antiformin I would emphasise the necessity for thoroughly washing the deposit left after centrifuging the specimen with saline, so as to rid it of all traces of antiformin ; as I found that two of the guinea-pigs died after a few days, and there was nothing to account for the death (cultures were negative) apart from the action of antiformin, as these specimens were imperfectly washed before being inoculated into the animals.

The next step was to select a medium-sized healthy guinea-pig, weight about 300 grammes, since this is, in my experience, the most suitable weight, as the smaller-sized and less mature animals did not appear to be able to survive the lowered resistance resulting from the X-ray exposure and inoculation.

The X-ray exposure appears to lower the resistance of the animals to every detrimental influence, such as cold, environment, insufficient feeding (a few of the guinea-pigs died as the result of the heating apparatus in the animal house being temporarily out of order. Other guinea-pigs in the same house not

X-rayed survived the resulting lowered temperature). It is, therefore, important in order to get good results to place the experimented animals under the most favourable conditions, special attention being given to such points as the feeding and the heating and cleanliness of the cages.

Previous to inoculation a blood film was taken from the guinea-pig's ear and a differential blood count was made, for comparison with the blood count after exposure to X-ray, in order to establish the depression in the lymphocyte count and its extent. The guinea-pig was then placed in a ventilated cardboard box of such size as to prevent it moving, and exposed to the X-rays. The animal in the box was placed twelve inches from a Coolidge tube. A five milliampere current was used, backing up $12\frac{1}{2}$ inches of spark between the points, and the current was reinforced by accumulators. It was left exposed for a period of ten minutes, care being taken that an even degree of intensity of the rays was maintained throughout the exposure. After being X-rayed, the animal was inoculated with the material for investigation, either the same day or at some time during the next few days. The injection was made intraperitoneally, the bulk of the material injected amounting to 0·5 c.c. or 1 c.c. The animal was then placed aside in a separate cage. A blood film was taken from the inoculated guinea-pig's ear every second day, and a differential or total blood count was made. The remarkable depression in the total white cell count and particularly in the small lymphocytes was evident from the very first. The blood count was followed in this way until the animal was killed, or had died as a result of the combined effect of the X-ray exposure and infection.

The length of time which elapsed before a positive result was obtained and tubercular lesions of the organs of the X-rayed animals at post-mortem were found varied from seven to fourteen days. The earliest positive result I obtained was in seven days and the average was about nine to ten days.

As will be seen from the annexed table, six of the guinea-pigs died within eight days, and the post-mortem showed well

marked tubercular lesions, especially in the mesenteric glands. One of the guinea-pigs I allowed to go on for 15 days with a view to finding out if the lymphocyte count was still depressed, and this I found to be so, as I have recorded elsewhere. The lesions found were most marked in the spleen, liver, and mesenteric glands, and in one case at the site of inoculation on the visceral layer of the peritoneum. The spleen in most cases was enlarged, and in many of them had well developed tubercles varying in size. The most marked changes were found in the mesenteric glands; very many of these were much enlarged. The largest glands were found between the coils of the large intestine and these I found were the most favourable for making film preparations. The glands were soft and caseating and readily broke down when crushed between two slides in making film preparations. The liver showed the presence of tubercles in six of the animals examined post-mortem, the tubercles varying in size from a pin-point to the head of a pin.

The coils of the intestine were often matted together, and in one case I found a small abscess between the coils of the large intestine. Having taken a number of films from the mesenteric glands, liver, and spleen, I examined these for tubercle bacilli. I repeatedly used the cold method of staining with these films with satisfactory results. Many of the films readily disclosed the presence of the tubercle bacilli, and others after searching for some time. (My results were confirmed in all cases by an independent worker.)

Controls were used in only five of the experiments; one of these died five days after being inoculated. The post-mortem did not disclose any obvious cause of death. The remaining four died, one in 21 days, one in 19 days, one in 17 days, and one in 16 days. All four showing tubercular lesions in the spleen, liver, and mesenteric glands, I did not consider it necessary to use controls after the first few experiments, as I was able to demonstrate the efficacy of the method in my third experiment with a tubercular sputum.

In order to obtain good results it is well to inoculate the material into the guinea-pig on the same day as it has been X-rayed. My practice was to send the animals which were to be inoculated to the X-ray Department in the morning and have the material injected in the afternoon

The results obtained fully confirm Morton's observations, as the six selected examples shown in Table I. demonstrate. From these results it may be assumed that, given an inoculum rich in tubercle bacilli, the experimental animal may be destroyed within 14 days with tolerable certainty that macroscopical tuberculous lesions will be found post-mortem.

One of the points elicited by Murphy (Journ. Exper. Med., 1914, 20, 397) in his earlier experiments is summarised in the following statement:—

"If the lymphoid system of an adult animal be depleted by exposure to X-rays, the animal loses its power of resistance to heterologous tissues and transplanted tissues are thereby enabled to grow readily within its body."

My own observations on the guinea-pig tend to show that this lack of resistance extends not only to the strangers within the gates—the inoculated tubercle bacilli—but also to its relationship to the external world, and many failures at the commencement of the investigation are to be ascribed to this cause. As examples may be cited, guinea-pig 1, which died within 24 hours from acute bacillus coli peritonitis, the control animal, identical in weight and injected with a similar quantity of sputum, remained alive for three weeks before it succumbed to general tuberculosis; and guinea-pigs 8, 9, 10, 11, 12, 13, all inoculated with the same material died within 48 hours of acute streptococcic septicæmia; and guinea-pigs 24, 25, 27 and 28, which were found dead, within a few days of inoculation (one of these animals was inoculated with cerebrospinal fluid, and another with fluid from a pleural effusion) (not shown in the tables), in the morning following particularly cold nights in February of this year, whilst similar sized animals in adjacent cages were unaffected.

TABLE I.

Guinea Pig.	Material Inoculated.	Result of Inoculation of X-rayed G.P.A.	Post-mortem Lesions.	
			Naked Eye.	Microscopical.
A	1·0 c.c. Sputum crowded with B. Tuberculosis	Killed after 16 days	Spleen enlarged, no tubercles seen. Liver no tubercles. Mesenteric glands everywhere enlarged, soft and caseous	T.B. present
B	Sputum	Killed after 15 days	Spleen enlarged, with tubercle present. Tubercles on liver. Mesenteric glands everywhere enlarged, soft, caseous, breaking down easily	T.B. present
C	Sputum	Killed after 14 days	Spleen much enlarged. Tubercles on the liver. Mesenteric glands everywhere enlarged. soft and caseous	T.B. present
D	Sputum	Killed after 13 days	Spleen normal. Caseating nodules found on liver. Numerous soft caseating enlarged mesenteric glands	T.B. present
E	Sputum	Killed after 11 days	Tubercles on liver and spleen, latter much enlarged. Mesenteric glands everywhere enlarged, soft and caseous	T.B. present
F	1·0 c.c. Urinary deposit (catheter specimen)	Killed after 12 days	Small tubercles on the spleen, which was much enlarged. Mesenteric glands, several enlarged, soft, caseous, easily breaking down	T.B. present

The earliest date at which naked-eye manifestations can be obtained has not yet been determined exactly, but a number of early deaths up to the end of five days followed the inoculation of sputum literally crowded with tubercle bacilli, when no lesions were observed and no tubercle bacilli could be demonstrated microscopically (see Table II.).

The most striking examples of early generalisation of bacillus tuberculosis in these X-rayed guinea-pigs are to be found in Table III.

A point which has been dealt with by previous workers in experimental inoculations of tubercular material is the extreme variation in the length of the period which elapses between the actual inoculation and the death of the guinea-pig from general tuberculosis. This time limit depends upon two factors:

1. The virulence of the tubercle bacilli inoculated.
2. The number of tubercle bacilli inoculated.

Wyssokowitscz (using tuberculous sputum) found that the fewer the organisms inoculated into the guinea-pig the longer the course of the disease before it was terminated by death and also if too few tubercle bacilli (less than 150) were inoculated into the rabbit, the disease was not set up. Koch also insisted on this point, and Theobald Smith recorded a few definite experiments to demonstrate it. He used an emulsion of a culture of bovine bacillus and injected it intravenously into a rabbit in a dose of 0·5 c.c. The remainder of the emulsion was diluted ten times and another rabbit was inoculated with 0·5 c.c. of this dilution. The first rabbit died of general tuberculosis in 26 days, the second dying 36 days after inoculation. It follows, therefore, from these observations that in order to successfully establish the presence of the tuberculous element in an inoculated specimen (by the ordinary method) the bacilli must be in sufficient numbers to set up the disease. If the bacilli are too few in number a negative result will follow, and, if they exist sparsely, the time limit for a fatal termination to the animal inoculated will be proportionately prolonged (in inverse ratio).

TABLE II.

Guinea Pig.	Material Inoculated.	Result of Inoculation of X-rayed G.P.	Post-mortem Lesions.		Control	Post-mortem Lesions.	
			Naked Eye.	Microscopical.		Naked Eye.	Microscopical.
G	Sputum	Died after 24 hours	Good deal of fluid in peritoneal cavity	Films from fluid and heart's blood showed the presence of B. Coli. No T.B. could be detected	Died after 21 days	Tubercular lesions found in spleen, liver and mesenteric glands	Films showed numerous T.B.
H	Sputum	Died 4 days after inoculation	Nil found	No T.B. could be detected	—	—	—
J	Sputum	Died in 5 days	No lesions found. Suspected to have died as a result of inoculation of antiformin	No T.B. could be detected	Died after 19 days	Tubercles found in liver, spleen and mesenteric glands	T.B. present

TABLE III.

Guinea Pig.	Material Inoculated.	Result of Inoculation of X-rayed G.P.	Post-mortem Lesions.	
			Naked Eye.	Microscopical
K	1·0 c.c. Sputum crowded with B. Tuberculosis	Died after 7 days	Pin-point tubercles on the spleen and liver. Spleen much enlarged. Mesenteric glands enlarged, soft and caseous	T.B. present
L	Ditto	Died after 7 days	Pin-point tubercles found on liver. Numerous enlarged, soft, caseating glands, which easily broke down	T.B. present
M	Ditto	Died after 7 days	Spleen enlarged. Numerous enlarged, soft, caseating mesenteric glands found	T.B. present
N	Ditto	Died after 7 days	Spleen enlarged. Mesenteric glands everywhere enlarged, soft and caseating	T.B. present
O	Ditto	Died after 7 days	Spleen somewhat enlarged. Numerous mesenteric glands, enlarged, soft and readily breaking down	T.B. present

TABLE IV.

Guinea Pig.	Clinical Diagnosis.	Material Inoculated.	Result of Inoculation of X-rayed G.P.	Post-mortem Lesions.	
				Naked Eye.	Microscopical.
P	Tubercular disease of intestine. Ulceration	Fæces	Died after 8 days	Spleen and liver not enlarged. Coils of intestine matted together. Small abscess found between coils of large gut. Mesenteric glands everywhere enlarged and soft	T.B. present
Q	Tubercular disease of the kidney	Catheter specimen of urine	Killed after 12 days	Tubercle found on the spleen. Numerous mesenteric glands, enlarged, soft and caseous. No tubercle on liver	T.B. present

The value of the method by inoculation of guinea-pigs exposed to X-rays must, however, be estimated by a standard of reliability, that is to say, it is not sufficient for the inoculation of material crowded with acid fast bacilli to give a positive result at an early date, it must be capable of giving evidence of the presence of bacillus tuberculosis even when the material inoculated fails to show the micro-organism after prolonged microscopical examination.

Two examples will suffice upon this point. In the fæcal material employed to inoculate guinea-pig (P) very prolonged search of the centrifugalised deposit after antiform treatment, resulted in the detection of one small bunch of acid fast bacilli; whilst careful search by several observers of the centrifugalised urinary deposit, subsequently injected into guinea-pig (Q) failed to show any acid fast bacilli whatever (see Table IV.).

Conclusions.

The existence of acid fast bacilli, other than bacillus tuberculosis in pathological material frequently necessitates resort to inoculation methods for the purpose either of confirming or excluding a diagnosis of tuberculous infection. Unfortunately the general utility of such tests is often discounted by the length of time which elapses before a definite result can be recorded.

Experience has already impressed upon us the advisability of employing the guinea-pig for inoculation purposes, since the introduction of even a few tubercle bacilli into this animal is followed by a definite sequence of events terminating in death from general tuberculosis at some period near to or remote from the date of inoculation (according to the number of bacilli injected, the type of bacillus, *i.e.*, human or bovine, the virulence of the strain, the site of injection and other factors), and varying from a few weeks to several months.

The deterrent effect of this time factor which operated so adversely against the universal employment of animal experiment in clinical laboratory diagnosis has stimulated research, having for its object the abbreviation of the "observation period" with, hitherto, but few tangible improvements on the methods of Marcet.

From the experiments made by me, with the material at my disposal, I succeeded in confirming Morton's results by the method of inoculation after exposure to X-rays. By this recent method we appear to possess a rapid and sure method of diagnosis of tubercular disease, and it cannot but strike one as a decided advantage to be able to arrive at an early diagnosis in those cases where a certain amount of doubt exists as to the presence or not of the tubercular element.

The technique of the method does not involve any more skill than the ordinary method. The apparatus required for carrying out the complete experiment is no doubt elaborate and perhaps costly, and necessitates the co-operation of the radiographer. However, in all big hospitals the apparatus is already installed for purposes of treatment, and this question of outfit does not arise.

The interesting question arises with this method as with the old method. Does a negative result absolutely and definitely preclude a diagnosis of tubercular disease? I should be inclined to think that a negative result while going a long way towards excluding tubercular disease, need not mean in all cases that the disease is absent. This method, however, could be repeated at once, where the clinical symptoms are equivocal, and by the repetition little time is lost before the second investigation is completed. I should say that two negative results thus obtained would be fairly conclusive evidence that one was not dealing with any active tubercular trouble.

I should like, in conclusion, to record my sincere thanks to Dr. Eyre for giving me facilities for working in the laboratory

of Guy's Hospital, and also for the valuable advice and co-operation afforded me by him during the progress of my investigations. I should also like to thank the laboratory assistants and also Dr. King Brown who very kindly confirmed the results I obtained.

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CASES OF ENTAMŒBA HISTOLYTICA INFECTION IN BRITISH RESIDENTS.

By

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The comparatively large number of cases of *entamœba histolytica* infection which have been treated in this country has excited a more wide-spread interest in this disease, and the large number of investigations which have been necessary for proper treatment of the cases has been fruitful in suggestions for further work. One of the interesting points which have been raised is the possibility of the existence of carriers, or actual infections, amongst the civil resident population. The carrier question has been brought forward in a paper by Yorke, Carter, Mackinnon, Matthews, and Smith;* who describe the results of examining for intestinal protozoa 344 persons who have never been out of Great Britain. Of the total, they found 2·9 per cent. contained cysts morphologically identical with those of *entamœba histolytica*. Some of the cases were young recruits in a military camp who had been associated for about two months with men who had returned from the Mediterranean. In these the percentage of positive results was higher than that found in the purely civil population (surgical cases in the wards of the Royal Liverpool Infirmary). The figures were 3·9 per cent. and 1·4 per cent. respectively. The difference may

be significant, though the numbers are small, to draw any final conclusion from; but it seems clear from their results that there are a certain number of carriers amongst the civil population. That the strain is a pathogenic one is also indicated, since these observers succeeded in infecting a kitten which developed a typical amœbic dysentery which progressed steadily to a fatal termination. If the number of carriers is as high on the average throughout the country, as would seem from the results of these workers, it is to be expected that cases of *entamœba histolytica* should occur occasionally in persons resident in Great Britain. And yet the recorded cases are few.* Several possible explanations suggest themselves. That the carrier question is not a serious one may be dismissed, since it is contrary to fundamental principles. That cases of this kind are known to occur and are not thought of sufficient interest to be worth reporting seems highly improbable. It would, therefore, seem that cases are being passed over unrecognised, and are, on that account, being improperly treated. That this possibility represents the true state of affairs is rendered probable from the following cases which have recently come under our notice. It is thought desirable to place them on record, for it is felt that our experience cannot be unique; and it is of the first importance that cases of this kind should be recognised wherever possible, since, in this disease, once a correct diagnosis is made, there is a reasonable prospect of cure, and without it cases may resist treatment indefinitely. Moreover, there are grounds for believing that on demobilisation the number of carriers in the country may be seriously increased.

Case 1.—W. S., æt. 38 years, admitted to hospital on June 29th, 1917. The patient stated that he had never been out of the country, nor had he been in contact with relations or friends

*See Worster Drought and Rosewarne, Brit. Med. Journ., May, 1916, p. 715, where further references may be found. The total number of certain cases appears to be three.

who had been abroad. He first suffered from diarrhœa in December, 1914. The disorder came on gradually, and he soon noticed blood in the motions. He came up to hospital and was treated at Out-Patients without any permanent benefit. He was admitted to Job ward where a sigmoidoscopic examination was carried out in 1916. He was transferred to John ward where he was treated as a case of "ulcerative colitis," and he received a course of vaccines. Blood never disappeared from the fæces, but it varied in amount from time to time. He was ultimately discharged and attended Out-Patients, where he received various forms of treatment again without permanent benefit. Bismuth relieved the pains, but blood and mucus persisted. Charcoal was of no value in treatment.

On admission, apart from the alimentary disorder, nothing abnormal could be made out, and the case was regarded as one of "ulcerative colitis." However, on examination of a stool it was found that there was a large amount of fluid containing very loose fæcal matter, pus cells, red blood cells, and small collections of blood-stained mucus. More detailed examination of these patches of mucus showed that living amœbæ were present, and that many of these contained red blood cells. In addition, a few free amœbæ were then found in the more fluid portion of the stool.

The case was therefore reported as one of amœbic dysentery. Further specimens were obtained, examined in the fresh state, and films were made and stained. The presence of amœbæ of the histolytica type was confirmed.

A suspension of the mucous clumps in the fluid accompanying the fæcal matter was injected into a kitten per rectum. In the course of four days the motions from the kitten became loose, and on the sixth day they were streaked with blood and a few living amœbæ were found. Still later the blood and mucus became more abundant and amœbæ could be demonstrated with great ease.

As soon as possible after the case was diagnosed as one of amœbic dysentery a course of emetine injections was begun.

In three days a striking improvement was observed and the amœbæ became few in number in the stools. A few days later none were to be found, and the motions became much better formed. On the tenth day of the course the patient, who had been complaining of the discipline of the ward, took his discharge from the hospital, and the case could not be followed further.

There can be no doubt that the patient was suffering from amœbic dysentery, and probably had suffered from this disorder since December, 1914. It is, of course, impossible to be certain that the previous disorder was also due to an amœbic infection, as it is conceivable that an amœbic infection developed on the top of an ulcerated colon due to some other infectious agent. In favour of this is the fact that the case was carefully investigated at the time of the previous admission to hospital. It is felt, however, that the single pathology is the more probable, and this view is borne out by the fact that there was never any cure or even great improvement till emetine treatment was begun. As regards the previous examination, it must be remembered that amœbæ were not specially looked for, and it is an organism easily overlooked unless careful search is made for it. We have to confess to having failed to find it when it was suspected to be present.

If this view of the single pathology in this case be accepted it will be observed that the case ran a very chronic course over a period of about 18 months. This may possibly be associated with a low virulence in the strain of amœba, since the infection in the kitten also ran an unusually chronic course. After the dysentery in the kitten had lasted for a little more than a week the animal appeared to recover, but a relapse occurred, and amœbæ were passed in numbers once more and the usual symptoms returned. For about fourteen days the infection seemed to be well established, but once more the infection slowly cleared up, and on this occasion the recovery was complete. Throughout this time the animal was never really ill, and it put on weight and grew well. This chronic course is

CASE 2.

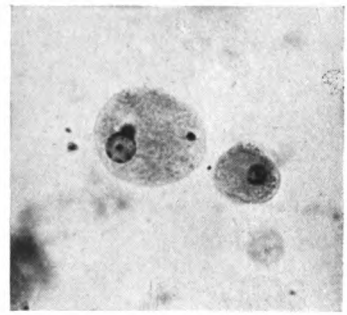


FIG. 1.

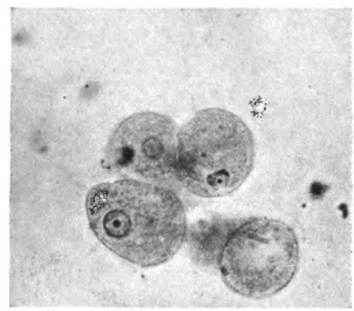


FIG. 2.

Figs. 1 & 2. Photomicrograph of amœbæ. Film preparation from kitten's cæcum. Case 2.

FIG. 3.

FIG. 4.

Figs. 3 & 4. Camera lucida drawing of cysts from fæces. Case 2.

All Figs. approx. 900.

unusual in the cat, as, once infection is established, the usual result is a continuous progress to a fatal termination.

Examination of the kitten's fæces for cysts after all acute symptoms had subsided always gave negative results. Post-mortem there was a little enlargement of the lymph follicles in the cæcum and a few areas in the mucous membrane with excess of small round cells and fibrous tissue, but the epithelium was intact and there was but little evidence of previous ulceration. No amœbæ or cysts could be found.

At one time the amœba was suspected of being morphologically different from true histolytica because the nuclei in the stained preparations from the patient presented some abnormal features. The chromatin was not evenly distributed on the nuclear membrane, but was irregularly clumped around the karyosome. Examination of further specimens from the patient, and from the kitten, and the submission of specimens to Mr. C. Dobell put the matter beyond all question. The abnormal forms were partially degenerate or poorly fixed specimens, and "plenty of quite typical *entamœba histolytica*" were also found.

Case 2.—G. D., æt. 48 years, admitted to hospital on August 16th, 1917, for lumbar and abdominal pain. Five years previously the patient was in the medical wards of the hospital. The records of the hospital show that a diagnosis of acute nephritis and alcoholism was made. The nephritis cleared up and the patient was discharged. There were no intestinal symptoms at that time to suggest any dysenteric condition. The patient was very unintelligent and gave vague replies to questions. He was certain that he had never been abroad, nor, as far as he was aware, had he been in intimate contact with those who had visited other countries. The present illness appears to have developed insidiously, as no adequate history could be obtained.

On admission the patient was flushed, restless, and emaciated. Pulse, 116; respiration, 24; temperature, 100°. The liver ap-

peared to be greatly enlarged and extended below the costal margin as low as the umbilicus. A point of burning pain and tenderness was found at the area under which the gall bladder might be expected to be, with a liver of this size. The pain radiated towards the lumbar region and the back. There was no jaundice. The bowels were loose and occasionally green coloured. Blood was never noticed in the motions.

On August 21st a laparotomy was performed by Mr. Hughes, and an enormous abscess was found immediately under the peritoneum. On opening this, "literally pints" of pus came away. The abscess cavity was very large and appeared to invade the liver in several directions. The cavity was drained and tubes inserted.

Bacteriological examination of the pus was negative, cultures remaining sterile after incubation for 72 hours. Inquiry as to the reason of the sterility of the pus was made, and only then, for the first time, was the possibility of amœbic abscess considered. Although considered to be unlikely, it was thought worth while to exclude the possibility. Examination of the pus on the dressings was made on August 25th, and no definite amœbæ could be found. Some large, hydropic cells, with vacuoles, were seen, but they could not be identified as amœbæ with certainty. On the 27th a specimen of stools was examined for amœbæ and cysts with negative results. However, in view of the appearances noted in the first specimen of pus from the dressing, both these examinations were repeated. On August 30th numerous cysts of *entamœba histolytica* were found in the fæces, and on September 5th, 6th, and 7th the examination of sterile saline wash-outs of the abscess cavity showed that fair numbers of living, active *entamœba histolytica* were present.

On the 7th September a course of emetine hypodermically was commenced and continued till the 16th. Under this treatment the amœbæ soon disappeared from the abscess cavity and the discharge rapidly diminished. Cysts were present in the stools in large numbers on September 20th, so a course of emetine bismuth iodide was started on the following day. It

was prescribed in pill form lightly coated with salol. This was continued until October 2nd. Under this treatment the cysts disappeared from the fæces for some days, but they returned in large numbers on the 8th October, when a few free, minute, precystic forms were also detected in the living state.

While a short rest in treatment was being given, and a consideration of what other steps were advisable was being made, the patient announced that he must leave the hospital, and no arguments would shake his determination. This case also was therefore lost sight of before the final result was established.

On September 3rd an emulsion of the amœbic cysts collected on the 30th August was fed to a small kitten. No infection resulted.

On September 5th a small amount of the saline wash-out from the abscess cavity, containing living amœbæ, was injected into another kitten per rectum. On the fifth day following the injection a little blood and mucus was passed. A few amœbæ were found. The symptoms subsided and the kitten recovered, apparently completely.

On the 20th September both the above kittens were fed with amœbic cysts from the patient's fæces. These, it may be noted, were collected after the course of emetine injections was completed. In both cases after five days blood, mucus, and amœbæ were passed in quantity. One kitten was killed on the seventh day, and in films prepared from the ulcerated surface of the cæcum numerous amœbæ, indistinguishable from *entamœba histolytica*, were found. The other kitten was killed on the eleventh day as the disease was progressing steadily. In this case, again, in films and sections, typical *entamœba histolytica* were found in large numbers.

Case 1 shows that amœbic dysentery may be quite chronic in character, and that when of this type it may possibly be overlooked. It might be used to support the theory, which has recently been resuscitated, that "ulcerative colitis" is actually amœbic dysentery or else amœbic in origin. It is a tempting

view, as by means of it many features of the disorder could be explained; but so far as I am aware direct proof is lacking. It is, of course, highly improbable that this case is unique, and thus it is the more desirable that further study of "ulcerative colitis" cases should be made, and that all amœbic cases should be excluded from the mass. With this idea, all cases of "ulcerative colitis" are regarded as suspect and a hunt for amœbæ is made. Only six or seven cases, two of which came to post-mortem, have been investigated up to the present, with negative results. The distinction is not always easy to make. It is quite common, in fact, it is the rule, to find cells in ulcerative conditions of the colon, which, through degenerative processes, simulate amœbæ; and it is only by careful examination that the truth can be arrived at. It does seem that the characters of the motions are different in the two conditions. The mere fact that one undoubted case was recognised is presmuptive evidence that the distinction is possible. As far as data go at present it would seem that in "ulcerative colitis" the motion is more uniformly fluid, more uniformly and intimately mixed with blood, contains more pus cells and leucocytes, and does not contain, as a rule, separate clumps of mucus. Ultimate appeal, however, must be made to the presence or absence of amœbæ, and it is here that difficulty may arise. A large, vacuolated, hydropic, body cell may easily cause errors. A distinction may be made through the discovery of intermediate forms showing partial vacuolation and less degeneration. Finally, an injection into a kitten's rectum may be made if amœbæ are still suspected. A negative result will not always exclude the possibility of the original being amœbic dysentery, but a positive result is conclusive. For this test, and for the direct examination, it is advisable to use as *fresh* material as possible, because amœbæ degenerate and die within a few hours, in most cases, after being passed.

Case 2 illustrates the value of pushing investigation till a definite diagnosis is arrived at, and suggests that liver ab-

scesses, even in this country, should be suspect till a definite cause is found. Also that an anchovy paste appearance is not an essential feature of the contents of an amœbic abscess.

The two cases occurring during such a short time indicates that these infections are probably being missed elsewhere. This view is supported by the fact that Dr. Perdrau showed me (also within the past year) sections of a solitary ulcer in the colon about an inch and a half across, and an abscess in the liver, from a post-mortem on a woman who had never left the country. In both sets of sections it was possible to demonstrate the presence of amœbæ indistinguishable from *entamœba histolytica*. Further, it is felt to be exceedingly improbable that these cases are of local occurrence, more particularly when the results of the Liverpool workers is remembered.

It was, therefore, thought advisable to put these cases on record in order that the attention of others might be drawn to the possibilities suggested above, and in order that other cases might be detected earlier and adequate treatment provided. Further, the possible increase in the number of carriers owing to the war must be borne in mind, and all possible opportunity be taken to treat such cases early and vigorously.

SUMMARY.

Three cases of *entamœba histolytica* infection in British residents are recorded. In two instances the infection was transmitted to kittens, in the third the evidence is merely histological.

It is suggested that cases of this type are not so rare as might be thought from the literature. And that cases of ulcerative colitis, colitis, and liver abscess should always be examined with a view to excluding amœbic infection.

I desire to tender thanks to Dr. Beddard, Mr. Hughes, and Dr. Perdrau for their kind permission to publish these notes of their cases.

A CASE OF PERIARTERITIS NODOSA.

By

H. C. CAMERON and P. P. LAIDLAW.

Examples of the disease known as periarteritis nodosa are quite uncommon. Up to the present time only 42 genuine cases have been recorded, and of these only two cases are English ones. The majority of the others have been recorded by German workers. Some confusion has occurred at times as to the characteristics of the disease, through the inclusion of examples of localised periarterial thickening, which on closer investigation prove to be cases of syphilitic periarteritis. Because of this confusion alternative names have been suggested from time to time. For example, "polyarteritis acuta nodosa" was favoured by Carnegie Dixon in his paper on the subject. But there is no general consensus of opinion in favour of the alternative names, and as most recent workers have employed the name periarteritis nodosa, we have adopted it in this communication.

The name periarteritis nodosa really describes the pathological picture met with in cases which come to autopsy. The disease itself appears to be an acute infection of obscure nature with the most varied complex of symptoms. The infectious agent leads to the formation of numerous, multiple, small, localised, thickenings on the walls of the smaller arteries. These nodules are apparently produced by acute inflammation and degeneration of all coats of the vessels, resulting in the formation of multiple, small, aneurysms. Repair and proliferative changes complicate the picture, and infarction, necrosis, or hæmorrhage, may occur in the organ or tissue supplied by the artery.

We have had an opportunity of studying a case of this type clinically, and examining the lesions post-mortem, and consider it advisable to put the case on record. It cannot be claimed that any new fact of importance has been brought out by the study of the case, and much useful information has been missed, because the condition, as is usual, was not diagnosed during life. Many points, therefore, on which particular information is desirable were not investigated, or even thought of in time. The post-mortem examination, though it established the nature of the affection did not shed any light on the ætiology of the disease. It is felt, however, that it is worth while to record the case on account of its rarity, and in the hope that such data as we possess may be useful to others.

No attempt has been made to review the other known examples of the disease as this has been done recently by others. Carnegie Dixon, 1908, Lamb, 1914, and Klotz, 1917, give very full accounts of cases and full information with regard to others. Reference to their papers will yield detailed information regarding most of the cases and full references to the literature may be found there.

Clinical Aspect of the Case.

C. G., a newspaper cyclist, æt. 27 years, came to me in the Out-Patient Department at Guy's Hospital on March 8th, 1916. He told me that he had always been in good health until a few months ago except for an illness seven years before for which he had been admitted to hospital and which he attributed to an accident while cycling. On consulting the hospital records, however, it was found that he had suffered from pleuritic effusion for which paracentesis thoracis was performed. The fluid drawn off remained sterile on cultivation, and the pleurisy was thought to be tuberculous in nature. He had felt no ill effects since. The present illness had begun some nine weeks before with attacks of severe abdominal pain which spread down the left costal margin to the back and shoulders. At first he had been sick on several occasions, but this had not been repeated re-

cently. He had been unable to sleep on account of the pain. For some weeks before I saw him the severity of the pain had been less, and his chief complaint at our first meeting was extreme weakness and a progressive loss of weight. Even then he was very thin and weighed only 6 stone 10 pounds. His height was not measured, but was approximately 5ft. 10in. His appetite was good, and he did not think that the pain was influenced by anything he ate or even by abstaining from food altogether. He was very thirsty. Physical examination was negative except for the following points which were duly noted in the clinical report. The radial arteries were abnormally thickened, having regard to his age, but were not tortuous. The urine was of low specific gravity, 1012, and contained a minute trace of albumen; no sugar; no indican; no blood by guaiac test. Gmelin's test negative. The heart was normal in size and position. The liver edge was palpable just below the costal margin, but the viscus seemed to be dropped rather than enlarged. There was distinct prominence of the lower dorsal vertebræ and the spine seemed to be held a little rigid.

On April 29th, eight weeks after admission, I first noticed enlargement of the cervical and axillary glands. The glands gradually increased in size, but at no time were they larger than almonds. They remained separate and freely mobile. On the same day he woke from sleep to find a musculo-spiral paralysis of the right hand and wrist due no doubt to accidental pressure on his emaciated arm.

On the whole, the weight continued to fall. He seldom complained of abdominal pain. His appetite was good, and he spent much of the day sleeping quietly. Early in May a slight œdema of the ankles and the lumbar region appeared and varied from day to day. The urine remained generally of low specific gravity and somewhat excessive in amount; in March the amount passed was generally over 60 ounces, sometimes over 70. In April the figure was generally over 100 ounces and sometimes over 120. On May 4th it reached 150 ounces. A trace of albumen was often found, but casts and pus cells

were never seen. The temperature, which was a little raised at first to 100° F., later became persistently subnormal.

The case excited a good deal of interest in the ward, and many diagnoses were suggested, to be abandoned in turn. At first I was inclined, on the grounds of the prominence and rigidity of the spinal vertebræ, the abdominal and vertebral pain, and the slight but persistent pyrexia, to consider the case to be one of tuberculosis of the dorsal vertebræ. A careful examination of the spine by the X-rays did not, however, support this view, and I was not able to elicit any spinal tenderness. Finally, I dismissed the slight kyphosis as due to his occupation as a newspaper cyclist.

The hardening of the radial arteries and the polyuria with a trace of albumen suggested an arteriosclerosis, perhaps of syphilitic origin, but the absence of cardiac hypertrophy and the extreme emaciation with slight pyrexia seemed to call for some other explanation. A Wassermann reaction was not carried out.

The enlargement of the glands above the clavicle and in the axillæ turned our attention to the possibility of malignant disease of the stomach and the intestines, but chemical examination of the stomach contents and the fæces, and the examination of the stomach and intestines after an opaque meal by the X-rays, did not support this view.

Addison's disease was considered, but there was no excess of pigmentation of skin or mucous membranes.

In the end no diagnosis was made other than polyuria and albuminuria.

H. C. C.

Summary of the Post-mortem Examination.

C. G., 27 years, May 30th, 1916. The body weighed 5 stone. There was obvious and striking emaciation. The superficial glands were enlarged. Deep scars of irregular shape were present on the prepuce.

The heart weighed 362 grm. and was free from superficial fat. Along the course of the coronary arteries, and the branches arising therefrom, were numerous small rounded masses, which in many cases were nearly spherical in shape. The largest of these was nearly 1 cm. in diameter and the smallest about 1 mm. On slitting up the coronary artery, which was in close relation to these, it was found that each of the small masses was in reality a small aneurysm. The largest of these was a saccular aneurysm with thick fibrous walls and communicated with the branch of the coronary artery by means of an opening 1·5 mm. wide. The cavity was filled with laminated blood clot.

The accompanying drawing shows the condition of the posterior aspect of the heart with the largest aneurysm in section and its communication with the artery. The other aspects of the heart showed a similar condition, but the aneurysms were not so numerous.

Further examination of some other of the nodules showed that they were in all probability completely organised aneurysms and at the time of examination consisted of masses of fibrous tissue. All the valves of the heart were normal. The heart muscle showed numerous small patches of fibrosis. The precise amount of this was not determined since it was desired to keep the specimen. In the anterior wall of the left ventricle just below the auriculo-ventricular junction there was a pale area of recent infarction, which measured about 2 cm. in maximum diameter. The roots of the large vessels were healthy.

The vessels of the lungs appeared to be normal. The vessels of the limbs and trunk were distinctly thickened and fibrous, but their general contour appeared to be normal. The vessels to the intestine, on the other hand, showed in addition to the general thickening numerous very small nodules at the extreme edge of the mesentery just before they entered the intestinal wall. These were only 1 mm. or less in diameter and could be more readily felt than seen. The large vessels showed no abnormality.

The kidneys together weighed 300 grm. and presented a very peculiar appearance. The surface was very irregular, and on stripping the capsule a surface consisting of smooth rounded bosses projecting from a rough granular background was seen. The depressions between the rounded masses, which were pale in colour, were dull red and granular. At these points the capsule did not strip easily, but it was not firmly adherent. On section the same variegated appearance was found, pale and dark patches alternating. The change was limited to the cortex. The vessels were prominent and fibrous in places, and at others were very difficult to find, their outline merging with the kidney substance.

The liver had an excess of fibrous tissue in Glisson's capsule, but the parenchyma was not cirrhotic. The arteries stood out from the cut surface as rigid tubes, and had unusually thick walls. They did not show any irregularities resembling aneurysms. An area 4 cm. by 3 cm. in the left lobe showed white infarction.

There was a general glandular enlargement throughout the lymphatic system.

The mucous membrane of the stomach was unusually thick and corrugated and showed a few petechial hæmorrhages. There was one small and quite superficial ulcer in the small intestine. No parasites could be detected in the bowel contents.

The testicles were very fibrous and scarred, and the tubules could be pulled out only at one point and that with difficulty.

The brain and other organs were normal. No lesion could be found in the cerebral vessels.

Microscopical examination confirmed the conclusions arrived at from the post-mortem appearances. All the main abnormal features found were readily explained on the view that the primary lesion was an arterial degeneration leading to aneurysm formation, and that secondary to this, there had arisen further degenerations in the parenchyma of various organs as the result of disturbed blood supply.

A number of small nodules in close relation to the branches of the coronary arteries were embedded in wax and serial sections cut, along the long axis of the vessels. A typical appearance is illustrated in Fig. 2, which is a photomicrograph of a section, stained with orcein and iron hæmatoxylin, approximately through the centre of the vessel. In two places, so close together as to seem on first inspection one, there is complete loss of all coats of the vessel. The absence of the elastic layers is very well illustrated by preparations of this kind. Surrounding the vessel, replacing the gap in the walls, and invading and replacing the lumen, is well-developed new fibrous tissue. In many of the preparations there was a great overgrowth of fibrous tissue around the vessel and even for some distance into the musculature of the heart. In a number of the vessels the lumen still persisted, or had been reformed, as a very minute channel through the new fibrous tissue which, as a rule, invaded the lumen extensively.

Some of the larger masses were dealt with in a similar manner, and various stages of organising aneurysms were seen. One of these showed a typical saccular aneurysm filled with clot which was only partially organised at the periphery and without thrombosis of the vessel from which the aneurysm arose. In all cases there was very little sign of active disease. There was no evidence of inflammation apart from the connective tissue reaction and a few small round cells aggregated in small clusters. In this respect the appearances differed from that usually seen in this disorder, and this is in all probability connected with the long history and chronic course in this particular case.

The kidney was a very beautiful example of the result of impaired blood supply. All stages of degeneration due to poor circulation could be found. Numerous areas in the sections showed patches of fibrosis with fibroid glomeruli and complete disappearance of the convoluted tubules resembling those met with in advanced arterio-sclerotic kidneys. Others, again, showed stages on the way to this condition, areas where the

kidney tubules were undergoing slow atrophy and a replacement fibrosis was beginning, while the glomeruli were comparatively unaffected. Other areas showed recent infarction. All these changes resulted from the impaired blood supply. In the majority of the vessels examined there was some abnormality to be seen. Some arteries showed extensive endarteritis and fibrosis around the outside of the vessel. Others showed, in addition to this, organising thrombi in the lumen. In these instances the endothelial lining was deficient. A few showed complete thrombosis of recent date. In a number of instances appearances similar to that found in the heart vessels were found. The wall of the vessel had given way locally, the lumen of the vessel, the gap in the wall, and the area immediately surrounding the artery were uniform masses of young connective tissue. Fig. 3 is another photomicrograph illustrating this point. Nowhere in the substance of the organ could be found definite aneurysms containing blood clot, and again there was no evidence of active disease in the vessels. The process had apparently reached a chronic stage and attempts at repair were in the foreground.

Sections of the liver were prepared through the infarcted area and in the immediate neighbourhood of this. The infarct consisted of shrunken liver cells, which were undergoing atrophy, but were just surviving. The nuclei, although imperfect in shape and staining, were fairly well preserved. The capillaries between the liver cell columns were almost empty of blood and contained very few red cells. At the margin of the infarct and the healthy tissue there was a typical leucocytic reaction, but the lesion was evidently not of sufficiently long duration to lead to any great connective tissue change. The branches of the hepatic artery, the bile ducts, and the portal vessels were embedded in a relatively very large amount of fibrous tissue. This was of recent formation, and only here and there, usually around the edges of the persistent liver lobules, were there collections of small round cells and leucocytes. The bile ducts were tortuous and enlarged, and there was evidence of the

formation of new small ducts at the edges of the liver lobules similar to those seen in examples of liver atrophy. The arteries showed the same picture which has already been described in the case of the kidney and the heart. The deficiences in the walls of the vessels were not so great, or so frequent, as in the case of the coronary vessels, but it could be found in a fair proportion of the diseased vessels. What was more striking in the vessels supplying this organ was the enormous overgrowth of the connective tissue of the intima. In many cases the artery was obliterated completely, and in others only minute central channels persisted. Considering the amount of the obstruction of the arterial supply to the organ, changes in the liver cells, such as fatty degeneration, were not at all striking. On the whole, the liver parenchyma was fairly normal. The cells were small and the capillaries relatively large and dilated. A few cells contained small vacuoles as the result of fatty degeneration.

It is to be regretted that owing to an oversight the intestinal vessels and the testicle were not preserved for section. It is thus impossible to say how far the fibrosis of the latter organ was due to infarction or chronic syphilitic lesions. Macroscopical appearances suggested the former alternative.

Summing up, we may say that the patient was probably syphilitic, and that he suffered from a vascular disease of uncertain origin, which was characterised by localised inflammation and degeneration of the vessel walls and the surrounding tissues, leading to the development of numerous small aneurysms on the smaller vessels of the heart, kidney and intestine. The disease of the vessels in turn brought about secondary degeneration in the parenchyma of these organs through infarction by clot, embolus, or by thrombosis ; or by fibrous tissue replacement due to ischæmia developing as intimal overgrowth became a prominent feature in the diseased vessels.

The greatest amount of change was seen in the kidney where only little normal substance was left, and it is thought probable that renal deficiency was largely responsible for the fatal

termination. The fibrosis and small infarction of the heart muscle, though doubtless important as contributory cause was not by itself sufficient to cause death. The importance of the renal insufficiency is also striking in the clinical report. The urine resembled that passed in cases of chronic renal fibrosis. It was of low specific gravity, of large and progressively increasing volume, contained traces of albumen, but no casts or blood. Unfortunately there was no investigation by chemical means which would prove inefficient excretion. In this time of stress many investigations which would give valuable results must be put on one side. The onset of œdema towards the close is also suggestive. The mode of death also agrees with this view. There was no sign of acute infection towards the end, and a blood culture post-mortem gave only a growth of bacillus coli.

The heart-beat during life was variable, but never excessively abnormal. It averaged about 80 per minute for weeks, and only at the beginning was it definitely rapid, 128 per minute. It was noticed that on a few occasions there were dropped beats which may have been associated with the fibrosis and infarction, but, on the whole, this was not a prominent feature.

There were no nervous symptoms.

Our case, it will be seen, is quite a typical example of the disease, but is much more chronic than the average one (over five months). There is no single case that gives a good impression of this disease, the signs and symptoms are so complex and different in different cases that it is hardly to be wondered that diagnosis is very difficult. And this is only what might be expected from the pathological picture. The main feature is a peculiar type of arterial degeneration which by itself will give certain symptoms; these will be overshadowed in many cases by degeneration of the parenchyma of the organs supplied by the arteries; and when it is remembered that there is no constancy in the group of arteries affected, it is evident that the symptoms must vary enormously in individual cases.

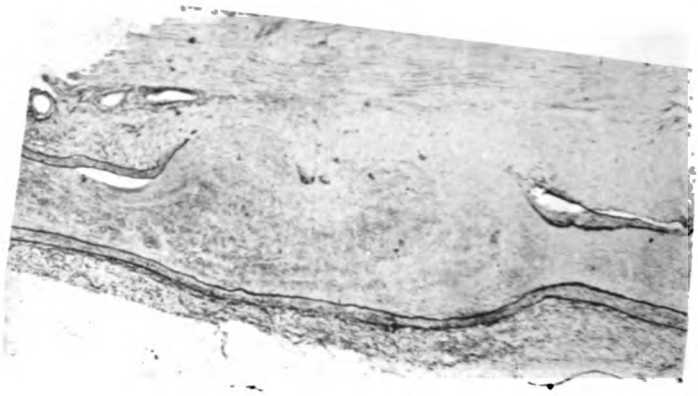
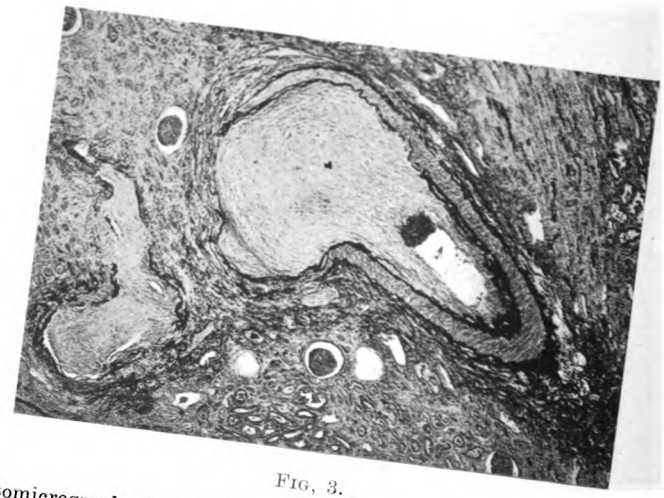


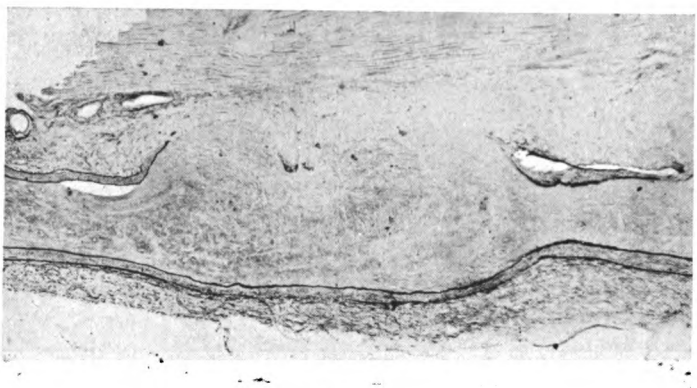
FIG. 2.

Photomicrograph of a longitudinal section of a branch of the coronary artery. Stained with orcein and iron hæmatoxylin. To show the rupture of the wall at two points.



FIG, 3.

Photomicrograph of a section of one of the kidneys stained with orcein. To show the rupture of the walls of the renal vessels.



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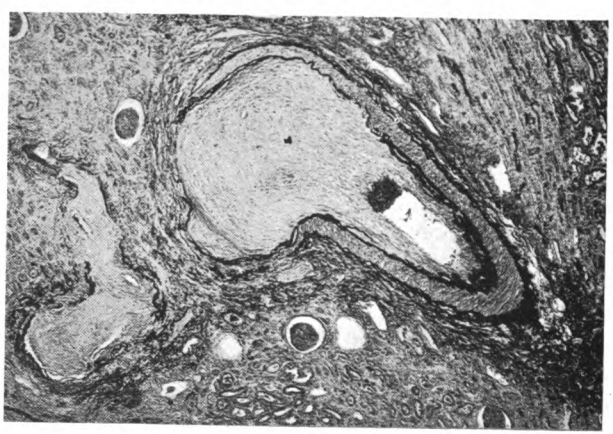

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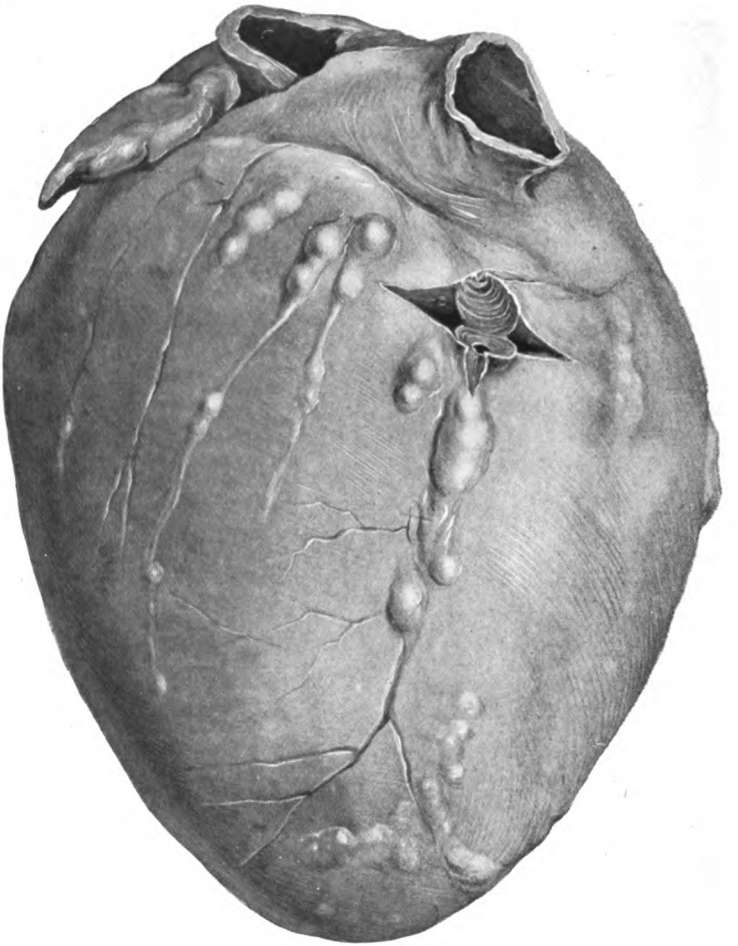

FIG. 1.

Wash drawing by Mr. Thornton Shiells of the heart. Posterior aspect. The incisions made at the autopsy have been for the most part neglected, and the heart depicted as seen on reconstitution.

Comparing our case with others, we see that the onset was not really acute, as is often the case. There was less temperature and fever than usually exists. On the other hand, the weakness, the abdominal pain, the wasting, the anæmia, the albuminuria were typical. No blood counts were carried out, so the usual leucocytosis may have been present in the acuter stages. It would have been very interesting to see if there was any eosinophilia, cf. Lamb, but this also was missed. More attention to the renal symptoms might have been of great assistance, but this also was neglected. The kidney lesions post-mortem were quite typical, but of a comparatively chronic type, cf. Dixon, Lamb, etc. The heart, though showing marked lesions at autopsy, gave rise to very few disturbances during life. This, again, appears to be usual. It is exceptional for cardiac symptoms to be present during life. The enlargement of the lymphatic glands, which was striking in our case, is not very common.

It is usual to attribute the vascular changes met with in this disorder to some infective process of obscure nature. Syphilis is apparently not the causative agent, since examples occur with no history of this disease and in the absence of a positive Wassermann reaction. In this connection it is worth noting that pieces of heart and kidney were stained by Levaditi's method, cut, and examined for spirochætes, but none could be detected. This result is in entire agreement with other observers. Some observers (Klotz) believe that syphilis may play some secondary part, predisposing to some other infection, but even this is doubtful. Streptococci have been suspected by some workers, and both Klotz and Lamb attempted to produce the disease in animals experimentally, but without success. For full discussion on the position of streptococci in relation to this disease the reader is referred to Klotz and Lamb. It may be noted, however, that there does not seem to be any very good grounds for incriminating this organism, and it is worth pointing out that both Lamb and Klotz failed to grow any organism from the blood during life, and Klotz also failed in the case of the local lesions, and this in spite of the fact that

they had fairly acute cases to supply any infecting organism that might be present. In our case bacilus coli was recovered from the blood post-mortem (as has been the case with others), but there is nothing of great significance in a result of this kind. A study of our case does not help very much in choosing between the various possibilities. The case ran such a chronic course, and all the post-mortem appearances and results of the study of the sections showed that repair was advanced; and the acute stage, when the exciting agent might have been present, was so far past that no conclusion can be drawn. The net impression of our case is a series of deficiencies in arteries and other organs made partially good by that ever ready material, connective tissue. This is in great contrast to some of the other recorded cases where there were signs of acute inflammation around the arteries and recent degeneration of the vessel wall. Even the study of these has failed to decide the causative agent, and there is the less reason to be surprised that the study of a chronic case should also fail in this respect.

The failure of the study of human material, and the failure to reproduce the disease in animals by inoculation of bacteria and material from human cases, has led to an appeal to comparative pathology. It was pointed out by Lupke that there was a corresponding, and possibly identical disease, in stags. From a herd he obtained numerous examples and studied them in detail. His results did not settle the cause. Careful histological examination of some of this material by Jaeger again failed to show any causative agent. The study of cases by Guldner and Joest occurring in a calf and a pig also were of no assistance in settling the matter. Going still farther afield a suggestion arises which may possibly be worth further attention, and that is, that the whole process may be due to a parasite and not a bacterium. It is a possibility that does not appear to one of us to have been sufficiently carefully excluded. It is well known that the multiple aneurysms in horses along the mesenteric vessels is due to a parasite *strongylus armatus*. In this case the disease begins in the inside of the vessel and pro-

duces atypical fusiform aneurysms. What is, perhaps, more significant is the case of aneurysms found in dogs which was recently studied by Haythorn and Ryan. Here it appears to be established that the aneurysms are produced by a nematode worm *spirocerca sanguinolenta*. The mode of attack on the vessel from without, the degeneration of the media, and the giving way of the wall resulting in aneurysm formation is most suggestive. It is unlikely that a parasite of this particular variety would have been overlooked in all the cases of periarteritis nodosa, but the idea of a bacterial infection has been so firmly held that it is conceivable that a larger parasite might be overlooked. The eosinophilia which has been noted, and is particularly emphasised by Lamb, and the local collections of eosinophile cells around the lesions at certain stages of the degenerations which have been noticed by many observers, is a small point which may be used to support the theory. Our case gives no data of value in this connection, but we repeat that the lesions were too old to be of any value in testing the point at issue.

One feels that what is wanted is the exhaustive study of a case which has been diagnosed during life in the acute stage, and in which the various suggestions could be tested in several ways. How long it will be before this occurs it is impossible to say, since it is a condition extremely difficult to diagnose successfully during life, unless, as has happened before, a nodule develops subcutaneously and this is excised for the purposes of diagnosis.

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MULTIPLE MESODERMAL MIXED TUMOURS OF THE UTERUS, ASSOCIATED WITH PLEURICENTRIC CARCINOMATA.

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According to the well-known theory of Cohnheim and its many modifications, cells which have remained unused during the development of a part, or that have been in some way thrust aside in post-embryonic life, form the nucleus from which many malignant tumours are said to be developed. These cells can either remain in their original situation, or be displaced and carried away to other parts of the body. They remain dormant for years and then suddenly spring to life. This theory is, of course, supported by evidence. Unfortunately, however, this is principally, if not entirely, furnished by tissues that, in post-embryonic life, become differentiated and rarely give rise to new growths. I refer to structures that performed a physiological function at some period of development and which, when they have served their purpose, usually disappear, but occasionally persist in a rudimentary condition. Chief among these are the remnants of the Wolffian body and duct. The former persists as the paroophoron, and as the tubules of the rete ovarii or epoophoron. Isolated parts of it give rise to the small cysts

broad ligament, to the anterior of which they are attached. The only tumours that are certainly developed from these structures, apart from simple cysts resulting from the accumulation of secretion, are the innocent adeno-myomata of the hilum of the ovary, and of the broad and round ligaments of the uterus. As the Wolffian body at the height of its development is an enormous organ, these remains have undergone little or no displacement. Analogous remnants are found in males, among which may be mentioned the small cysts of the epididymis that have been described by Meyer[23] in newly-born infants. In rare instances they are lined by squamous epithelium, and they are said to be of no practical importance, since they usually disappear. Mr. Rowlands and myself,[29] however, have published a case of primary squamous celled carcinoma of the epididymis, which we believed to have originated in cells of the epidermis that had adhered to the Wolffian duct. It is much more probable that its starting-point was one of these tubules of the Wolffian body. This is the only case, to my knowledge, in which this embryonic structure can be shown with any degree of certainty to have given rise to a carcinomatous new growth. The Wolffian duct persists in females as the more or less fragmentary duct of Gartner. Three or four cases of carcinoma of its ampulla have been described (*vide* Meyer[22]).

Another example of an embryonic structure which occasionally persists in man is the duct of the pituitary, as described by Erdheim.[5] Its remains are frequently to be seen as islands of squamous epithelium in the extension of the anterior lobe of the gland into the infundibulum. They are only found in adults, and grow slowly throughout life. They are probably composed of indifferent cells in children, and, therefore, cannot be recognised. They give rise to the rare squamous celled carcinomata of this organ.

I cannot refrain from mentioning the accessory pieces of suprarenal cortex that are frequently found on and in the kidneys. As they are parts of this organ which have adhered to the renal capsule during its development, they are not strictly

comparable with the persistent embryonic remains mentioned above. They are frequently quoted in support of Cohnheim's theory, as they are generally believed to give rise to the "hypernephromata" of the kidney. The evidence is, however, by no means conclusive. I need but refer to the recent paper on this subject by Ipsen,[17] which is a really conscientious effort to approach the question from an unprejudiced standpoint.

We see, then, that in all these instances the tissues undergo the maximum amount of development they are capable of. Only rarely can they be shown with certainty to have formed the starting point of a malignant new growth. Since these differentiated structures usually behave in this unsatisfactory manner, undifferentiated rudiments, consisting of more or less embryonic cells, are made use of in explaining the formation of tumours. They have been found to be particularly useful as an explanation for neoplasms, such as the one to be described below, which contain tissues quite foreign to the organ affected. When cartilage is found in a tumour of the uterus, the simplest explanation is that cells of the sclerotome have found their way to this region, provided some developmental mechanism exists by means of which they can be carried there. Although the mechanism is furnished in this case by the growth backwards of the Wolffian duct, there is no positive evidence that it ever carries such cells down with it. For even if they had been carried we should be unable to see them. As they are undifferentiated it would be impossible to distinguish them from the surrounding tissue. The following pages are occupied by an attempt to show that, however necessary the assumption of embryonic remains may be in many cases, in the present an alternative explanation is possible.

Clinical History.

A unipara, aged 55, was admitted to Guy's Hospital under Dr. Fawcett, to whom I am indebted for the history and for permission to publish the case, on September 20th, 1916, with a left-sided pleuritic effusion.

She gave a six months' history of pain in the chest, followed by shortness of breath, and had lost two stone in weight since the beginning of her illness.

Forty-two ounces of a blood-stained fluid were removed from the left chest. It contained an abundance of red blood corpuscles, a few leucocytes, and an occasional epi- or endothelial cell. A hard tumour was felt just above the symphysis pubis. It was diagnosed as a uterine fibroid. and the possibility of a malignant new growth of the uterus with pulmonary metastases was discussed. She left the hospital at her own request on October 26. There was not much improvement in her condition.

She was re-admitted on November 12th, when 40 oz. of blood-stained fluid were withdrawn from the left chest. It rapidly re-accumulated, and the following amounts were aspirated: On November 21st, 53 oz.; on December 5th, 50 oz.; on December 24th, 12 oz. She died on January 8th, 1917, nine months after the onset of the symptoms.

Abstract of post-mortem report.—Left pleura greatly thickened. Lung compressed and airless. Several firm white nodules of new growth under the pleura, involving the pulmonary tissue. Right lung emphysematous. General arterio-sclerosis. Liver with many small deposits of new growth. (None of these were kept for microscopic examination.) Kidneys granular with numerous small retention cysts. The appearance of the pelvic organs is described below.

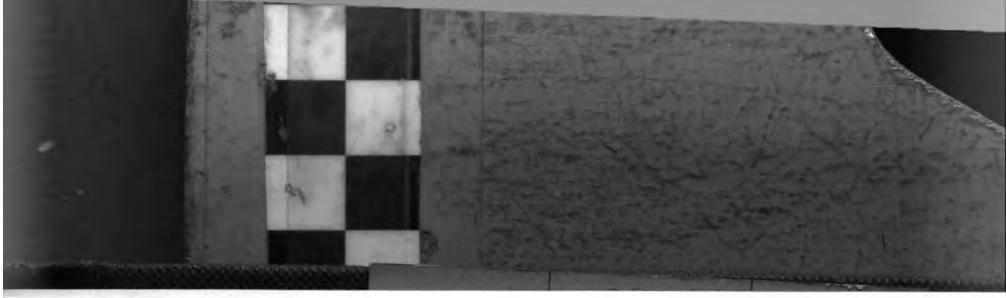
Description of Specimen.

Fig. 1.

The specimen consists of the uterus and cervix, with the Fallopian tubes and ovaries, and a piece of the bladder and rectum. The uterus is enlarged. It measures 15 c.m. from fundus to external os. It has been laid open by a longitudinal incision in the middle line of its posterior surface. Its walls are thickened, and the fundus is occupied by an oval intra-mural fibro-myoma with a large smooth-walled central cavity. The uterine cavity is dilated and triangular in shape. The two upper angles of the triangle correspond to the openings of the Fallopian tubes on either side of the fibroid of the fundus. The lower angle is formed by a pocket to the left of the internal os, and is occupied by the large tumour presently to be described. The mucous membrane is smooth in places. The greater part of its surface is, however, occupied by areas of slightly projecting small irregular granulations which, in places, form warty excrescences and give it a rough appearance. The cervix, which is pushed to the right, measures $2\frac{1}{2}$ c.m. in length. Its canal is not dilated. The external os is transverse and is marked by old superficial scars. On its posterior lip there is a small erosion. A plug of mucus projects through its orifice.

Within the uterine cavity, and projecting from its walls, the following structures are to be seen:—

1. A small flat papillomatous polypus, with an irregular granular surface (Fig. 1, B). It arises by a long fibrous pedicle from a linear fold of the mucous membrane of the upper part of the anterior wall of the uterus, 2 cm. to the left of the orifice of the right Fallopian tube.



2. A similar, but larger and less flattened papilloma (Fig. 1, C), 6 cm. in length, which arises by a broad flattened pedicle from a fold of the posterior wall of the uterus, on the same level as, but 1 cm. to the left of, the first polypus.

3. A triangular flattened growth (Fig. 1, D) with an irregular nodular surface. It measures $4\frac{1}{2}$ cm. in its longest diameter, and hangs down into the uterine cavity from its attachment, by a broad base, to the middle of the fundus.

4. On lifting up this tumour, the mucous membrane in its vicinity is seen to present a very granular structure. A small polypus arises in this area from the anterior uterine wall. It is narrow and flat, and measures barely 1 cm. in length, and shows no signs of branching. It was excised together with the underlying muscle for microscopic examination.

5. A large, roughly cubical tumour, 14 by $12\frac{1}{2}$ by 9 cm. in its longest diameters, which arises from the middle of the left wall of the corpus uteri (Fig. 1, E). It is firm in consistency, and its surface is occupied by a number of irregular linear fissures, which vary in depth and extent, and subdivide it into numerous prominent nodules. Its upper border is concave and was, in the recent state, moulded by the fibroid of the fundus. Below it occupied the pouch to the left of the internal os. Here it had exerted a pressure on the uterine muscle sufficient to cause thinning and sloughing of its wall. It projects for a distance of about 2 cm. into Douglas' pouch, the peritoneal covering of which is much inflamed, and presents several superficial ulcers and sloughs, besides a a few small nodular elevations. The most dependent part of the tumour is marked off into an oval boss, about 1 c.m. in diameter, by an annular constriction. It is probable that this fitted into the internal os during life. The tumour is mottled. Its general colour is yellow and pale pink. There are numerous streaks and patches of a grey translucent appearance scattered irregularly over its surface. There are present several small hæmorrhagic areas, especially over its lower part. On section the surface is uniform, and is mottled with small hæmorrhages and the cross-sections of blood vessels.

The pedicle of the tumour, which is just below the level of the opening of the left Fallopian tube, consists of a fold of the uterine wall and is marked on the peritoneal surface by a funnel-shaped depression. The muscular bundles of which it is made up run for some distance into the tumour, which overlaps its stalk like the head of a mushroom, to lose themselves within its substance.

It is to be noted that these tumours are quite superficial at the level of the uterine mucous membrane and that they present only slight signs of infiltration of the muscle.

The left round ligament is shortened and thickened. Both the Fallo-

"hydatid of Morgagni" is attached to the abdominal ostium of the left tube, and there are two small cysts close together in the broad ligament of this side, near the tubal attachment and 3 cm. from the lateral border.

The right ovary is enlarged and measures 8 cm. in its longest diameter. It consists of a few large thin-walled cysts, with a pseudo-mucinous contents. Its surface is covered by bands of confluent raised papillomatous vegetations, some of the largest of which have become distended to form small grape-like vesicles. They chiefly occupy the depressions between the cysts, and gradually fade away as they reach the most prominent points of the latter.

The left ovary is enlarged to a lesser extent than the right. Its base is hard and infiltrated, and its free border is occupied by a few pseudo-mucinous cysts. Its surface is covered by granular patches similar to, but less well developed than those on the opposite ovary.

On the peritoneal covering of the bladder there are several superficial rounded and linear patches of flat granulations, the largest of which have a yellow centre.

The bladder and rectum are healthy.

Microscopic Appearance.

1. *The uterine mucous membrane.*—Sections were examined from numerous parts of the smooth and the granular areas.

In the regions that are smooth to the naked eye, the mucous membrane is atrophied and reduced to a thin layer of loose connective tissue, in which a few round, oval, and stellate cells, and the remains of the uterine glands are to be seen. The great majority of these are flattened, and reduced to slits, whose long axes lie parallel to the surface. Others are distended into small cysts filled with mucin. They are lined by a single layer of compressed, cubical or flattened epithelium. The surface epithelium is often absent, or bands of flat and cubical cells, some of which are being desquamated, are all that remain of it.

In the next stage the mucous membrane, which is still smooth, increases three or four times in thickness. It now consists of a network of delicate fibrils, which mostly run parallel to the surface, and whose meshes are occupied by a faintly granular albuminous substance, which does not give the reactions of mucin. The connective tissue cells are fairly numerous. They are round, oval, stellate, and spindle-shaped, and have no tendency to collect in groups. Isolated cells with short rod-shaped nuclei are not common. The blood vessels are abundant, and are mostly thin-walled capillaries. Budding by means of angioblasts is to be observed in some of them.

At about this stage changes occur in the epithelium. The flat or cubical cells on the surface of the mucous membrane increase greatly in all their dimensions. They acquire a tall columnar, cubical, or round shape. Their nuclei proliferate and arrange themselves in two or more layers,

without coincident division of the cytoplasm (Fig. 2). Long club-shaped masses are thus produced. The free ends of the clubs are often subdivided by incomplete longitudinal constrictions, and the nuclei undergo division at the same time, so that small multinucleated lobulated syncytial masses result. In adjacent cells division is complete. These usually occupy the spaces between the proximal ends of the syncytia. Others are pushed outwards by cell proliferation. Local heaping of cells and stratification result. The nuclei are mostly very large and oval. They contain one or more large nucleoli, are bounded by a thick membrane, and traversed by a delicate network of chromatin. Other nuclei are small, and give one the impression that they have resulted from unequal direct division. Others, again, are cylindrical or pear-shaped and intensely basophile. Their state of preservation is not sufficiently good for an opinion of the number of the mitoses to be formed. Pyknotic nuclei are common near the surface.

Similar changes occur in the epithelium of the more superficial of the uterine glands. As it is possible, in sections taken from numerous parts of the uterus, to observe appearances that are to be regarded as transitions between the flattened uterine epithelium and the large irregular cells, these changes must have occurred independently at many points of the mucous membrane.

The epithelial cells are strongly basophile. Both in this respect and in their large size they present a striking contrast to the more or less atrophied remains of the old uterine epithelium. They are sharply marked off from the stroma, but there is no basement membrane. Cilia are nowhere to be seen.

Some of the largest of the cells possess a clear, less basophile and slightly more acidophile cytoplasm than do the others. They also show slight indications of fibrillation. It is, therefore, possible that they are very young squamous cells, although I have never seen any more definite characters in them. They only occur on the surface.

In this way the uterus acquires a new epithelial covering. It is smooth at first. Very soon, however, small connective tissue papillæ begin to project from it. They increase in length and send off branches, which are mostly narrow, delicate, and very vascular. Their connective tissue corpuscles resemble those that have been described above. Collections of small round cells, with little or no cytoplasmic covering, make their appearance. The epithelium is folded over the connective tissue papillæ, and projects between them as irregular gland-like structures. They are shallow at first, but soon deepen, and are subdivided by small secondary papillæ. The stroma grows farther out into the uterine cavity, the folding and branching of the epithelium becomes more complicated, until an adenomatous structure results. This consists of irregular branched cavities, tubular glands, and cystic spaces. They are all lined by tall columnar epithelium, which forms a single layer, or nearly fills the lumen. No signs of infiltration are to be observed. The granular naked-eye appearance of the mucous membrane is in this way produced.

The proliferation reaches its maximum over the pedicle of tumour E, and around the base of tumour D. Here the mucous membrane is occupied throughout its entire thickness by large glandular acini filled with columnar cells, and with many papillomatous projections into their lumina. This formation extends up to the muscle, a few of the most superficial of whose fibres are to be seen in the septa between the acini. These septa consist of a delicate spindle-celled stroma, with the remains of compressed uterine glands (Fig. 3). The new epithelium spreads within the old glands.

2. *Polypus B* (Fig. 1). — It consists of delicate branched connective tissue papillæ covered by tall epithelium, which is very similar to that on the uterine mucous membrane. It forms irregular spaces and tubules, all but the smallest of which contain numerous cross sections of papillæ. The *epithelium* has no tendency to infiltrate the stroma. It forms a single layer on its surface with local heaping of cells, which occurs principally at the bottoms of the crypts and tubules. Syncytia can be seen, but they are not often met with. The *stroma* is loose, with a few fine fibrils and numerous cells. Among these small round cells with dark nuclei occur in groups. Large vesicular oval nuclei, besides spindle, irregular, and long rod-shaped ones are scattered about irregularly. The centre of every papilla is occupied by a wide blood vessel, the walls of most of which are limited to a layer of endothelium. A small amount of condensation of the stroma has taken place around some of the largest. The reaction for mucin is negative in the connective tissue.

3. *Polypus C* (Fig. 1).—This tumour is composed of broad connective tissue papillæ, which enclose highly irregular convoluted and branched spaces. The *stroma* is far in excess of the epithelium. It contains numerous cells separated by a matrix of a homogeneous myxomatous appearance, which bears a strong resemblance to embryonic connective tissue. Where the matrix is most fully developed and the cells are consequently few in number, it gives a distinct mucin reaction with mucicarmine. It is noteworthy that the adipose tissue presently to be described is always most abundant at such spots. The cells of the stroma are most numerous on the surface of the polypus and around the tubules, where they often form a distinct subepithelial layer. Cellular areas occur in the deep parts as well. The cells differ considerably in shape. Their nuclei are usually large and vesicular, and round, oval, or irregular. One finds scattered among them a few deeply-stained small round, long and short spindle, and rod-shaped nuclei. Capillaries are very abundant here; they are wide and usually distended with blood, and their walls consist of a layer of endothelium. The myxomatous change is best marked towards the centres of the papillæ. The matrix swells. The cells are identical with those of the subepithelial zone, but many stellate forms make their appearance. All parts of the connective tissue contain a number of giant cells with large lobed nuclei. In serial sections the most superficial of these can be traced to the epithelium which lines the tubules. They are connected with it and each other by cytoplasmic processes. It is probable that all these giant cells are epithelial elements that have

invaded the stroma, and whose nuclei have undergone swelling and partial cleavage. A few bundles of connective tissue, with distinct fibrils and narrow nuclei, are found in the deeper parts of the papillæ and around the large blood vessels that occur here.

The most interesting member of the connective tissue group in this polypus is the adipose tissue. It is found as small lobules near the centres of the papillæ (Fig. 6). Isolated fat cells may, however, occur everywhere in the stroma. It is quite easy to follow the development of this tissue from the embryonic stroma, some of the cells of which are large, with oval or crescentic nuclei and granular cytoplasm. Two or more small round spaces appear inside them. They increase in size and coalesce, the nucleus at the same time becoming much flattened and pushed to one side. Typical fat cells result. Shallow ulcers and small hæmorrhages are common on the surface. The adipose tissue here presents appearances identical with those observed in fat necrosis.

The *epithelium* covers the whole of the polypus, with the exception of the ulcerated areas, and forms a lining to all the numerous long branched tubules and spaces which permeate its substance. It consists typically of a single layer of cells, which vary from a tall columnar to a flattened shape. The nuclei are oval, and are often bounded by a coarse membrane surrounding what appears to be an empty space. The epithelium is very much like that on the mucous membrane of the uterus (Fig. 4). It is flattened over the prominent parts of the tumour, and is very tall in its tubules and bays. Stratification is often to be observed over wide areas. In such places there is a distinct tendency to superficial infiltration of the stroma. The syncytia and the irregular cells described under 1. are numerous. Beautiful great goblet cells filled with mucin occur almost everywhere. Small crypts and tubules are given off, and the epithelium is obviously in a very active state of proliferation. That this is so is shown by a change that was hinted at in the uterine mucous membrane, but can here be studied in great perfection. This is the appearance of squamous among the columnar cells. They are found on the surface and in the tubules, and can at once be recognised by their large round shape, their big vesicular nuclei, and their clear eosinophile cytoplasm. Intraprotoplasmic fibrillæ are present in some of them. They never present intermediate forms which would lead one to suppose that they are produced by a metamorphosis of the adjacent columnar cells, which are never found between them and the stroma. They occur singly or in groups, some of which are large; they may even form complete linings to tubules. Often these squamous cells become flattened and surround a large central cell, an arrangement characteristic of the cell nests so often met with in pathological conditions of the epidermis. No prickle cells were found, but a few cells were observed to contain numerous granules of keratohyalin around their nuclei. Keratinization occurs freely, and the lumina of the tubules are often occupied by shreddy masses of non-nucleated horny scales.

4. *Tumour D* (Fig. 1).—This bears a strong resemblance to C, and need not be described in detail. The tubules are fewer in number. They

are deep and branched. The *stroma* is more highly differentiated than in C. The myxomatous change has extended throughout its greater part, and large areas, especially near its base, stain a diffuse pink colour with mucicarmine. Broad bands of fully differentiated fibrillar connective tissue are found around the large vessels, and often split the myxomatous tissue into incomplete lobes. No plain muscle was found.

The lobules of *fat* are very large, whole fields of the microscope often being wholly occupied by this tissue. One small nodule of typical embryonic *hyaline cartilage* was found. Its cells are surrounded by wide capsules, separated by a small amount of hyaline matrix. The edges somewhat suddenly shade off into the surrounding stroma, which is very mucoid, and contains a few round and spindle cells.

Areas of definite *sarcoma* are met with. They are of two kinds. The first consist of small scattered patches whose cells have undergone proliferation, and present the appearance of a large spindle-celled sarcoma. The other are very much larger areas of small round cells with an alveolar arrangement within the meshes of a delicate stroma. Among the cells a few larger spindle and stellate forms and some multinucleated small giant cells are to be found. These areas have a strong tendency to infiltrate the surrounding structures, and flourish exceedingly in the fat.

Another kind of giant cell is found in a restricted area. Here one sees very large oval or irregular, intensely eosinophile isolated bodies which often send out one or more processes. They contain a number of irregular or oval nuclei, that are either collected at the centre, or form a ring around the periphery of the cell. Long multinucleated bands and big spindles are obviously of the same nature. Their cytoplasm is sometimes faintly longitudinally striated. In a good many it appears to have undergone some sort of degeneration, as it is broken up into flakes, between which there are numerous vacuoles. In spite of the fact that these structures show no signs of transverse striation, I have no doubt whatever that they are embryonic *skeletal muscle* cells and fibres. They are imbedded in an almost structureless mucoid stroma (Fig. 8).

The *epithelium* is the same as that of polypus B. The squamous epithelium here reaches its highest stage of development. It forms a complete lining to some of the tubules, and is made up of a cubical Malpighian layer, a stratum mucosum with prickle cells, and a layer of flattened horny cells, which are often desquamated. The columnar epithelium contains large numbers of goblet cells (Fig. 6). It has a marked tendency to infiltrate. At one spot on the surface of the tumour near its base it invades the stroma as long branched glandular processes that are lined by one or more layers of very tall cylindrical cells. This spot has all the characters of a differentiated adeno-carcinoma of the uterus. The basal cells of the tubules everywhere infiltrate the connective tissue. This invasion is particularly strong in areas of sarcomatous proliferation of the stroma, where tubules and solid buds of but slightly differentiated epithelium are intimately mixed with the connective tissue elements (Fig. 5). The epithelium is far more typical

in structure on the surface than in the deeper parts of the tumour. The goblet cells and the most highly differentiated squamous cells are only seen in the former situations, and the diffuse infiltrations are limited to the latter. I may here mention a small tubule whose lumen is completely surrounded by a ring of protoplasm in which there are no traces of cell outlines. At intervals clusters of nuclei occur, which produce bulgings of the cytoplasm into the lumen (Fig. 6).

At the base of the tumour there is considerable fibrosis of the uterine muscle. The new growth extends for a short distance only into its superficial layers, in the form of processes of homogeneous connective tissue. It has given rise to a certain amount of splitting of the muscular bundles, the remains of whose cells can be traced for a short distance into its substance.

5. *The small, tag-like polypus* under tumour D is an early stage of development of C and D. The uterine mucous membrane in its neighbourhood has a papillomatous structure, and consists of numerous branched glands, which run more or less at right angles to the surface, and abut on the muscle. They are lined by columnar epithelium. The stroma is reduced to a minimum. It has a fibrillar matrix, with spindle cells and numerous capillaries. As the base of the tumour is approached, the papillæ increase greatly in thickness owing to homogeneous swelling of the matrix. The epithelial cells become more irregular in size, and a few isolated, definitely squamous, cells make their appearance among the columnar cells of the tubules. The polypus arises by a narrow pedicle from about the middle of this altered part of the mucous membrane. Beyond its pedicle it broadens considerably. Its matrix becomes more and more homogeneous and swollen, and gives a faint mucin reaction. A curved bundle of uterine muscle has been dragged outwards by it, and extends for some distance into its substance. The epithelium over its surface is composed of flat and short columnar cells. There is, however, a large area of squamous epithelium immediately below its attachment. The apex is capped by squamous epithelium, some of the cells of which contain granules of mucin. These have run together in a few of the cells to form goblets, whereas the bodies of others are stained a bright red with muci-carmine. The "squamous" nature of these cells is proved by their containing intra-cellular fibrils.

6. *Tumour E* (Fig. 1). — At first sight this presents a totally different appearance to D, in that the sarcomatous elements are now developed at the expense of the other tissues and dominate the picture. The homogeneous embryonic stroma is especially abundant near the base of attachment. It is generally more cellular, but otherwise does not differ essentially from that already described. Owing to proliferation of its cells an alveolar sarcoma is produced. This shows a marked tendency to invade the vessels, within which it extends for a short distance between the bundles of the uterine muscle. It splits them up, and their remains can be traced for varying distances into the tumour. Other spots have the structure of a spindle-celled sarcoma. They usually con-

tain narrow bands of plain muscle, whose nuclei are long and rod shaped, and show transitions to the oval nuclei of the sarcomatous cells. Strands of fibrous tissue occur. Fat and striped muscle were not found.

The greater part of the tumour is necrotic. Between such areas, and especially around the blood vessels, there are broad strips of healthy tissue. This consists of myxoma and of alveolar sarcoma mingled together in a most irregular manner. The former gives a very strong mucin reaction. Many nodules of hyaline cartilage are scattered about in the peripheral parts of the tumour. Their centres consist of large cells with round and shrivelled nuclei (Fig. 7). They lie in spaces that are surrounded by definite capsules that stain a bright red colour with mucicarmine. Their cytoplasm is often reduced to processes which traverse the cavities radially from the nucleus to the capsule. These cells occur in small groups with more or less of a hyaline matrix between them. At the periphery of the nodules of cartilage the connective tissue corpuscles can be seen to swell, to become rounded and separated by an increasing amount of matrix. These islands vary greatly in size. Some are microscopic, others can readily be distinguished with the naked eye, as the semitranslucent areas described in the macroscopic appearance of the specimen. These large nodules are generally entirely necrotic.

The *epithelium* is very much less in amount than in D, and is almost entirely restricted to the base, where it forms a lining to a few wide, irregular, branched, tubular spaces. Infiltration is marked. Many solid and tubular epithelial formations are present in the deeper parts of the stroma, some of which can be definitely located inside lymphatic vessels. The periphery is devoid of an epithelial covering. Here, however, one meets with small collections of cubical (*i.e.*, altered columnar) and of squamous cells, the latter of which are often keratinised. They occur in the midst of the myxoma and the sarcoma. Such collections, when they consist of squamous cells, closely resemble cartilage, but can be differentiated from it by the fact that they do not stain with mucicarmine. The groups of cubical cells often contain mucin. As this always occurs as globules and round bodies within spaces, formed either by a single cell or surrounded by epithelium, it is in most cases easy to distinguish them from the elements of the stroma.

The *pedicle* consists of fibrotic uterine muscle. A few of the blood capillaries in its deepest parts contain emboli of new growth, some at least of whose cells are definitely epithelial in character.

I may here state that the uterine muscle in general shows no appreciable changes.

7. *The fibroid at the fundus* (Fig. 1, F) is a cellular fibro-myoma. The central cavity is lined by a thin layer of œdematous connective tissue, on the surface of which an occasional flattened endothelial cell is found.

8. *The ovaries.*—The structure of the papillomata on the surface of both ovaries is very similar to that of polypus C. These outgrowths

consist of branching papillæ of homogeneous embryonic connective tissue, which is much more œdematous than in the uterine tumours. In places it gives a faint mucin reaction. The centres of the papillæ are usually occupied by a differentiated fibrous stroma. They are lined by columnar epithelium, in the midst of which there are patches of squamous cells. This epithelium, which usually forms a single layer on the surface, has grown down into the deeper parts of the left ovary. It has infiltrated its substance in the form of large papilliferous cysts and spaces, whose lumina are often filled with cells. Many of these are necrotic. The spaces are surrounded on all sides by ovarian stroma. Even in the deepest parts they contain a few squamous cells.

The ovarian tissue is fibrotic and encloses the remains of old corpora lutea. The large, thinned-walled cysts contain a homogeneous coagulated fluid. They are lined by a single layer of small granular epithelium, which is often thrown into minute folds and flat papillæ. The smallest cysts can be traced to ovarian follicles. They contain a blood-stained fluid. Their lining is formed by an irregular layer of follicular epithelium, the most central cells of which assume a cubical form, and contain a few mucin secreting goblet cells among them.

9. *The left round ligament* (Fig. 10).—Its superficial layers are infiltrated with leucocytes. Its muscular bundles are separated by œdematous connective tissue. The arteries are greatly thickened; their intima has proliferated and has often occluded the lumen. A few small branched tubules and a minute cyst occur in the deepest part of the ligament. They are lined by a single layer of regular short cubical epithelium, with oval nuclei, and are imbedded in a small amount of stroma. This bears a strong resemblance to that of the uterine mucous membrane, and none at all to that of any of the tumours that have been described. Its cells are numerous and spindle shaped, and are separated from each other by wavy fibrillæ. This stroma, which shows no signs of œdema, contains numerous thin-walled capillaries, and gradually passes into the intermuscular connective tissue. The bundles of muscle in the immediate neighbourhood of this minute patch of mucous membrane present no signs of hypertrophy. If anything, they are smaller and less numerous than those nearer to the periphery of the ligament.

10. *The deposits on the peritoneum* of Douglas' pouch and of the fundus of the bladder consist of small masses of cellular stroma, whose surface is ulcerated and whose deeper parts gradually merge into the subperitoneal fat (Fig. 9). The cells are irregular in size and shape and are imbedded in an excess of homogeneous matrix, which is identical with that of parts of the uterine tumours. Capillary blood vessels are numerous, especially near the inflamed surface. The stroma contains a number of small irregular epithelial structures, some of which possess a distinct lumen. Their cells are cubical or flattened, consist of one or more layers, and have a tendency to project into the lumina in the shape of small papillæ. Epithelial cells also occur singly, or in small groups of three or four in the midst of the stroma. Others lie within lymphatic spaces.

Some of the epithelia in the deeper parts are calcified. These alone of all the structures of the nodules give a positive mucin reaction.

11. *The pulmonary nodules* possess a stroma which is cellular in parts. In others its matrix is homogeneous, and in yet others it is fibrous. It contains numerous irregular masses of alveolar sarcoma, and some tubules. The latter are lined partly by columnar, and partly by squamous epithelium, some of the cells of which are keratinized. The same tubule occasionally contains both kinds of epithelium, and is then often lined by one or two layers of basophile cubical or columnar cells. The squamous cells occupy the lumen, but, in a few tubules at least, touch its periphery at one spot.

The representatives of the connective tissue series that we have met with during the description of the case are: Cellular connective tissue, whose matrix often undergoes homogeneous swelling and gives rise to myxomatous tissue, fibrous tissue, plain muscle, round and spindle celled sarcoma, hyaline cartilage, fat, and skeletal muscle. The three last of these are of most particular interest, since they do not normally occur in the uterus, and never in its new growths, except in the small group of which the present is an instance.* This group is known as the "mesodermal mixed tumours" of the uterus, for reasons presently to be stated.

Literature.

I now propose to give brief abstracts of the cases of mixed tumours of the uterus that have been recorded. I shall limit myself to those that contain cartilage and that have arisen from the body of this organ, and shall not enter into an account of those of the cervix. Here I need only say that they are slightly more frequent in the cervix, upwards of a dozen having been described. They present no essential differences as regards structure and clinical history, except that they generally occur at an earlier age and, when they project into the vagina through the external os, have a tendency to assume a racemose form. In this respect they resemble the grape-like sarcomata of the vagina of children, which often contain striped muscle, but never

*This statement is not quite accurate. Fatty changes, apart from degeneration, occur rarely in uterine fibroids.

cartilage. The most complete account of mixed tumours of the cervix, with special reference to their pathology, is that of Kehrer.[18]

1. Geissler (9) describes a round and spindle-celled sarcoma with islands of hyaline cartilage. It was found in the lateral and posterior wall of the uterus in a woman of 50. (This description is copied from Gaebelein (7).)

2. Seydel (31) records a large compact polypus in an unmarried woman of 42. It arose at the junction of the body and the cervix, and was covered in part by uterine and in part by cervical epithelium. In addition to the hyaline cartilage, which formed by far the greater part of the tumour, there were found an embryonic indefinite stroma, areas of round and spindle-celled sarcoma, and bands of plain muscle. He concludes that the tumour is the result of incomplete imperfect differentiation of the indifferent stroma in several directions.

3. Gebhard (8) gives an account of a large pedunculated tumour of the fundus of a XI-para of 56. Under the microscope it was seen to be made up of connective tissue, plain muscle, fat, hyaline cartilage, endotheliomatous tissue, and areas of round-celled sarcoma whose origin he traces to the endothelium. There were present uterine glands, and squamous epithelium with cell-nests, which presented no signs of carcinomatous proliferation.

4. Penkert (27) observed a soft, partly cystic, pedunculated tumour of the fundus of a X-para aged 62. It contains young connective tissue resembling granulation tissue, myxoma giving rise to hyaline cartilage. plain muscle, fibrous tissue, and sarcoma with giant cells. Uterine glands with cystic dilatations, adenomatous, and early adeno-carcinomatous changes are present. Areas of carcinoma and possibly of endothelioma occur as well. The stalk of the tumour contains the differentiated innocent structures, whereas the malignant changes occur at the periphery. He regards his case as a true mixed tumour of the nature of a teratoma.

5. Hunzicker (16) reports on a II-para of 58, on whom hysterectomy had been performed. She died five months later of a large local recurrence. The primary tumour is polypoid, and arises by a broad pedicle from the anterior uterine wall at the level of the internal openings of the Fallopian tubes. The stroma consists of a round and spindle-celled sarcoma with numerous transversely striated embryonic muscle cells and fibres, which are best developed in the pedicle. The peripheral zones contain fairly large masses of well differentiated hyaline cartilage, with capsules and transitions to the sarcoma. Fat cells are present as well. As they possess no nuclei, he concludes that they are not true adipose tissue, but result from fatty degeneration. The tumour is incompletely covered by uterine mucous membrane, which shows extensive metaplasia into thick layers of typical squamous epithelium with numerous mitoses, but without keratinization. On the outer surface of the uterus there is

a secondary deposit with well-developed striated muscle. Almost everywhere the uterine walls and those of the cervix contain nodules of sarcoma and of skeletal muscle. The recurrence is a spindle-celled sarcoma with poorly formed striped muscle and no cartilage.

6. Gaebelein (7) has written a dissertation on a large polypoid tumour which springs from the lower half of the body of the uterus of an VIII-para of 50. Its structure is that of a myxo-sarcoma with hyaline cartilage, of which one island only was found. It also contains plain muscle with direct transitions into the sarcomatous stroma. A large recurrence in the pelvis six months later consists largely of hyaline cartilage, which arises from the cells of the myxomatous stroma.

7. Murray and Littler (24) had removed a tumour that had grown diffusely as bosses and polypi over the mucous membrane of the greater part of the uterus in an unmarried woman of 46. There is no infiltration of the muscle. Microscopic examination shows a heterogenous collection of tissues, ranging from simple connective tissue through varying degrees of malignancy to an irregular celled sarcoma; tissue resembling myxoma, but really an œdema, as no true myxoma staining reactions are found; hyaline cartilage; gland tissue, probably persistent uterine glands; and fat. A superficial simple papilloma and some follicular cysts are present in the right ovary. No recurrence a few months later.

A full list has recently been published by Glynn and Bell[10] of uterine tumours with skeletal muscle. I have here mentioned those only in which cartilage was found.

These seven cases resemble the present one in that they all contain hyaline cartilage and areas of sarcoma. An embryonic stroma is noted in the majority. In several instances the mucin reactions are positive. Other tissues of frequent occurrence are connective tissue, plain muscle, and fat. Striated muscle occurs once only together with cartilage. Endotheliomatous areas, due to proliferation of capillaries, are noted in two instances.

Except in Penkert's[27] case, the epithelium was always present as a partial covering to the surface and to the remains of glandular spaces. It was always typical of the uterus or cervix and showed no signs of active proliferation, although an amount of growth sufficient to keep pace with the stretching of the mucous membrane over the tumour had no doubt occurred. Squamous epithelium was found twice; in Hunzicker's[16] case it is abundant, and its cells in a state of active division.

Penkert[27] alone describes a hyper-proliferation of the epithelium, ending in adenomatous and carcinomatous growth. Unfortunately his descriptions of these changes are very brief, and he has made no attempt to work them out adequately.

The ages of the patients are of interest. The youngest was 42 and the oldest 62 years of age. The average is 53 years, which corresponds very closely to that of the present case.

All these cases differ from the one that is now under consideration in that the primary growth was solitary. (In that of Hunzicker[16] alone there was a metastasis under the peritoneal covering of the uterus, and in the one of Murray and Littler[24] the greater part of its mucous membrane was involved.) The distinguishing features of our case are the presence of smaller isolated tumours in other parts of the uterus, and the peculiar changes to be observed in its mucous membrane.

I will state at once that, for reasons to be given below, I do not regard these smaller tumours as metastases of the greater. I consider them to be independent neoplasms, that owe their existence to the same causes that produced the latter, and that only differ from it in their lesser degree of maturity.

Changes in the Uterine Mucous Membrane.

It will be necessary to begin with a discussion of the changes that have taken place in the uterine mucous membrane. This is, in part, atrophic. The remains of the glands are compressed, and the epithelium is flattened and desquamated. The stroma is loose and slightly œdematous, and is poor in cells. These changes are due partly to the pressure exerted by the large tumour, and partly to the involution that is normal at the age of the patient. They are of the nature of a senile and atrophic endometritis. The epithelium that has escaped damage has proliferated in order to cover the raw surfaces that have resulted from cell death and desquamation. Proliferation is excessive from the start. The regenerating cells are large, acquire irregular shapes, and their nuclei undergo rapid direct division

and bands of protoplasm result (Fig. 2). Some of the largest and heaviest syncytial masses exert a pull on the stroma, which is dragged towards the cavity of the uterus. Small papillæ arise. They increase in size and send off branches. The epithelial proliferation keeps pace with the growth of the connective tissue papillæ, if it does not exceed it. It extends to the remains of the uterine glands. Adenomatous formations result (Fig 3). Owing to folding and invagination of the tubules, highly complicated papillomatous growths are produced, the largest of which is represented by polypus B.

While these changes are going on in the epithelium, the stroma becomes more cellular and acquires new capillary blood vessels. The connective tissue corpuscles are scattered about at first, but after a time they show a tendency to group themselves into small masses.

This amount of regeneration, though large, does not exceed that which takes place under physiological conditions, such as after menstruation and in pregnancy. It must be remembered that the uterine mucous membrane is subjected during life to a good deal of injury, to which it responds with great rapidity. After the separation of the membranes in child-birth, for instance, the superficial layers of the spongy stratum of the decidua are cast off by the formation of a line of demarcation. This passes as much as possible through the flattened superficial parts of the uterine glands. Between these raw connective tissue septa remain. They are rapidly covered by the epithelium of the glands, which glides over them and proliferates by amitosis. Syncytia are found in the deeper glands. These syncytia of uterine glands were first described by Schmidt[30] in a case of ectopic gestation. Syncytia, very similar to those I have described and figured, are recorded by Werth[33] in the mucous membrane after curetting. (A comparison of his Fig. 13 with Fig. 2 of this paper shows that some of them are identical in appearance.) Even the adenomatous areas around the base of tumour E have their physiological prototypes in the deep glands in pregnancy. These are large and dilated, with tall columnar

epithelium and true papillæ, *i.e.*, such as possess a connective tissue core. Again, the invasion of the superficial layers of the muscle is not greater than that which is to be seen in many specimens of endometritis.

Although on account of their structure I have called these formations adenomata, it must be understood that they are not, as yet, true new growths, but rather the expression of an intense regenerative hyper-proliferation of the epithelium.

Nowhere between the attachments of the tumours are there signs of infiltration of the uterus with structures resembling those of the new growths.

The Stroma of the Tumours.

The next stage is seen in the small simple polypus described above under 5, in polypus C (Fig. 1), and in parts of D and E. Here the stroma becomes swollen and acquires a homogeneous appearance, which is due to an accumulation of fluid within and between the fibres. At first it does not give a mucin reaction, later, however, the presence of this substance can be demonstrated after staining with mucicarmine. The reaction is faint at first, but increases in intensity until it reaches its maximum in the superficial parts of E. This is a sign of differentiation; the older the tissue, the more mucin does it contain. The connective tissue corpuscles are diminished on account of the swelling of the matrix. They assume irregular shapes; stellate cells with processes, characteristic of embryonic tissue, are met with. This resemblance has been laid stress on by all the writers on the subject. In the present case it is very striking. Some authors have found mucin, others have not. This discrepancy is due to the state of development undergone by the tissue in the different cases, since we have seen that the mucin is most abundant in the peripheral parts of the biggest tumour. (The stroma, in various degrees of differentiation, is shown in Figs. 4 to 8.)

It is important to note that the change occurs in the mucous membrane of the uterus over a relatively wide area around the

narrow base of the small tag-like polypus. This area, which is clearly defined and covered by typical, although greatly proliferated, uterine epithelium, is not raised above its surroundings. It shades off distinctly, although rather suddenly, into the surrounding connective tissue. It has not compressed it as it would have done if it had possessed an expansive independent method of growth. It is clear that this area is the result of a change in the direction of the formation of myxomatous tissue undergone by the stroma of the mucous membrane itself.

The stroma has reached a certain amount of differentiation by the time it has become myxomatous. It is never very cellular except at the periphery of E, where it is intermingled with sarcoma, to which it gives rise by the proliferation of its cells. Here it also produces the nodules of hyaline cartilage. At suitable spots its cells become large and rounded. The matrix between them increases in amount, forms spaces for them to lie in, and is condensed as capsules around the oldest cells of the nodule. The capsules give a strong positive mucin reaction (Fig. 7). They consist of chondro-mucin. Other cartilaginous islands have ceased to grow, and have become surrounded by a thin, usually ill defined, zone of slightly condensed connective tissue. The whole of the cartilage is cellular. Its corpuscles often form irregular groups and, in a few cases, two or more are enclosed by the same capsule. A blood vessel is occasionally present within the islands I have never seen appearances in any way suggestive of commencing ossification, and regard the vessels as having belonged originally to the myxomatous tissue, and as persisting after its conversion into cartilage. The fact that it is only the fully differentiated myxoma that produces the cartilage explains why the latter is almost entirely confined to the biggest of the tumours. Only one small nodule was found in that next largest in size.

The formation of mucin is a differentiation of the embryonic tissue in one direction, and is associated with a decrease in the rate of proliferation. This is most intense before the change has become marked. It occurs over areas that, owing to the struc-

ture of their cells and the absence of definition at their edges, acquire all the characters of a round or spindle-celled sarcoma. The former, which usually possesses an alveolar arrangement, may assume large dimensions and infiltrate its surroundings. In D it has invaded the adipose tissue, the remains of which are found in its midst, and in E it is to be met with inside blood vessels. It occurs in the pulmonary metastases, but has probably been here developed in situ from their embryonic stroma. The spindle-celled sarcoma is nowhere abundant. At the base of E its cells elongate and its nuclei acquire a distinct rod shape. At this spot it has differentiated into plain muscle. It is of interest to note that this tissue was found nowhere else as a part of the new growth. The present case differs in this respect from the others recorded, in the majority of which it was strongly in evidence.

We have seen that adipose tissue, often in the shape of large lobules, is present in C and D, but that it was not found in E. As it is abundant in the former it is fair to assume that, if present at all, it must be so to a very much smaller extent in the latter. The fat cells can be traced to their origin from the cells of the embryonic stroma. They are large and acquire vacuoles, which increase in size and coalesce, finally to fill the whole of the cells. The nucleus is pushed to one side and becomes crescentic. When the fat is involved in the ulcers on the surface of C, it undergoes the changes characteristic of fat necrosis elsewhere.

Another tissue which is differentiated from the homogeneous stroma is fibrillar connective tissue, bands of which are found in various parts of D and E.

In a restricted part of D there are elements which I believe to be skeletal muscle (Fig. 8). They are imbedded in an almost structureless matrix, which shows signs of condensation into a kind of perimysium around some of them. Spindle cells occur in the stroma. Some of these are small and do not differ from similar cells in other parts of the tumour. Others are larger, and stain more deeply with eosin. It is these that are the

youngest muscle cells that can be recognised as such. Intermediate forms occur. Irregular large multinucleated masses are found, whose cytoplasm is vacuolated, and whose nuclei have undergone pyknotic changes. Long narrow bands with ribbon-shaped nuclei are common. They none of them show the least signs of cross-striation, nor are they surrounded by a structure comparable to sarcolemma. I have compared these bodies with the striated muscle of a mixed tumour of the kidney. If allowances are made for the differences in fixation, which is not good in the present specimen, they are identical with these in all essentials save in their want of striation. It is possible that they represent a very early stage of differentiation, one prior to the appearance of cross-striation, which is first seen in the fifth week of embryonic life. Again, the changes in the cytoplasm suggest some form of hyaline degeneration.

The distribution of these tissues is not uniform in our different tumours. The homogeneous and myxomatous tissues occur in all; hyaline cartilage, spindle-celled and alveolar sarcoma, and fibrous tissue in D and E; fat in C and D; plain muscle in E; and skeletal muscle in D. We have seen that these structures all originate in the homogeneous tissue. This resembles the mesenchyme of the embryo not only in structure, but in its ability to differentiate into a large number of members of the connective tissue group. Not only does it give rise to tissues that are normally found in the uterus and in its everyday connective tissue tumours, but also to such as do not occur in this organ, either in the adult state or at any period of its development. They are only found here in the mesodermal mixed tumours.

These mixed tumours differ in many essential respects from ordinary sarcomata. The latter consist of cells which are all the same in nature and reproduce their kind only. Their growing points contain nothing but undifferentiated young connective tissue or sarcoma cells. Where growth is less active a certain amount of differentiation may set in. It is always in the same direction and depends, directly or indirectly, on the tissue in

which the neoplasm has started. It may lead to the formation of cartilage or of bone, or even of both these tissues, or of plain muscle, but never to that of cartilage and muscle. As the myxomatous tissue plays so important a part in our tumour, it is well to mention that myxo-sarcomata occur. They are probably analogous to the other forms of sarcoma in which there has been only slight differentiation, and that in the direction of the primitive connective tissue of the embryo.

The Epithelium of the Tumours.

We must now turn again to the epithelium, which passes directly from the uterine mucous membrane into the tumours. It covers the entire surface of the polypi and of D, lines the numerous branched spaces that penetrate into their deep parts, and sends glandular processes into the stroma. It is only interrupted at points where superficial ulceration has occurred, and has disappeared in E except over its basal part. In structure it is identical in many places with the rapidly proliferating parts of the mucous membrane, the same irregularities in shape and size of its cells, and the tendency to the formation of syncytia being faithfully reproduced.

At first the epithelium forms a regular lining to the stroma. It consists of a single layer of cubical and columnar cells which, although they do not rest on a basement membrane, present a sharply-defined edge on their inner aspect and have no tendency to infiltrate. To form a covering to the tumours the epithelium must have kept pace with the increase in bulk of the subjacent tissues. This in itself necessitated a large amount of proliferation on its part. Consequently its cells have undergone all the changes we have seen in those of the mucous membrane. Another expression of this increased energy on the part of the epithelium is the occurrence of squamous cells. They are found everywhere on the surface, in the wide spaces, and even in the gland-like tubules. A single squamous cell is often found in a row of columnar cells, from which it is easily distinguished by

eosinophile body, and the fibrillation of its cytoplasm. The columnar cells differ in the smaller size and obvious reticulation of their nuclei, and in their basophile and granular protoplasm. I shall, therefore, refer to them in future as "granular" cells, a convenient term by which to distinguish them from the "fibrillated" squamous epithelium. Islands of the latter are common and vary much in size (Fig. 4). They are always directly applied to the stroma, have a tendency to become stratified, and therefore project outwards beyond the level of the single layer of granular epithelium. They undergo a certain amount of differentiation, which reaches its greatest perfection in tumour D. Prickle-cells, keratohyalin granules, and horn are produced, the latter abundantly. The horny cells are converted into non-nucleated flakes.

I cannot enter into a discussion of the theories of this metamorphosis of the uterine epithelium. It is an instance of indirect metaplasia. In the uterus it is only found in polypi and in association with carcinomata. In the latter it is of frequent occurrence. Thus, of the 15 carcinomata of the body that were operated on in Guy's Hospital during the last four years, only four were pure columnar-celled growths. Eight contained both columnar and squamous epithelium, which often occurred together in the same acinus. The three remaining cases were pure squamous-celled carcinomata. Metaplasia of the uterine epithelium is, therefore, always a sign of very active, if not neoplastic, proliferation. It is associated with some form of irritation. In order to protect themselves from the irritant, the epithelial cells to some extent acquire the characters of the tough epidermis. It is not the stable, fully-differentiated cells of the normal mucous membrane that can do so, but only the young, comparatively indifferent cells that result from active proliferation. It therefore follows that the patches of squamous epithelium in our case result from the growth of a single cell, and do not increase in size by a metaplasia of the neighbouring definitely granular cells. I have mentioned in the histological description that cells which I regard to be of this indifferent

nature occur in the mucous membrane. I have also seen them in the tumours. Owing to their very nature it is hard to describe them. They are not granular cells, nor are they fibrillar cells, but carry suggestions of both.

The goblet cells that are met with in large numbers (Fig. 6) are another sign of irritation and of hyperactivity of the epithelium. It should be noted that the epithelium of the tubules in which they are most frequent is very tall with rod-shaped nuclei, and bears a striking resemblance to that of the intestine. Another interesting fact is that the squamous cells, although they have become differentiated in a new direction, retain some of the characters of their parent tissue, as is shown by the secretion of mucus by them.

Malignant Changes in Epithelium.

These signs of active and even of excessive proliferation of the epithelium are associated with indications of the assumption of a definitely blastomatous habit of growth. It first becomes evident at the bottoms of the glandular spaces and crypts of polypus C. The granular cells become heaped into several layers and begin to grow downwards into the stroma. On account possibly of the novelty of being surrounded on all sides by connective tissue, some of them seem to be placed at a disadvantage. They are unable to divide completely, but form giant cells with lobed nuclei (Fig. 4). The majority acquire greater and greater powers of infiltration. Areas are found, consisting of tubules and solid processes of epithelium, in every way identical with an undifferentiated columnar-celled carcinoma (Fig. 5), and others in which the superficial cells have all the characters of those of a differentiated adeno-carcinoma of the uterus. Later still, isolated groups of granular and of squamous cells are found far away from the surface in E. Epithelial cells occur in the vessels of the muscular pedicle of E, and are again met with in the metastases.

Where it forms a covering to the surface, the epithelium grows in a perfectly physiological manner. It is in the deeper parts

of the tumours that it acquires carcinomatous characters. This explains its absence over the distal part of E, whose stroma is chiefly made up of rapidly growing sarcomatous tissue, with the expansion of which the superficial epithelium has been unable to keep pace.

Here, then, we have an unmistakeable instance of the pleuricentric, one may almost say omnicentric, origin of a carcinoma. A blastomatous mode of growth begins at all suitable spots. This phenomenon is, I need hardly say, in direct opposition to the idea of the origin of neoplasms from displaced embryonic cells. We see the epithelium assume malignant characters under our very eyes, and are inclined to curse our blindness for being unable to discern the cause of the change.

It is the granular epithelium only that acquires malignant properties. The squamous areas never show definite signs of infiltration. Where they are found as islands in the stroma and in the deposits in the lung, they are usually associated with granular cells. It is probable, therefore, that they have arisen by metaplasia of the latter in situ. That this can occur is proved by the behaviour of the epithelium in the ovary. Squamous are found among the granular cells in places where infiltration has extended into the depths of the ovarian tissue.

The Metastases.

All the metastases that were examined contain the epithelium as well as constituents of the stroma of the uterine tumours. Those of the ovaries are the largest, and copy the structure of the primary growths more faithfully than do the others. The epithelium is identical. It consists of a layer of granular cells, among which squamous islands are abundant. It forms a covering to the surface of the papillæ, and dips downwards in the shape of wide spaces and narrow tubules. In the superficial parts it presents no appearances of malignancy, but in the deeper crypts it begins to infiltrate. The infiltration is slight at first, and often takes the form of epithelial giant cells. Later it becomes very much more marked than in any one of the uterine

growths, and invades the ovarian tissue as large solid columns and cystic spaces lined by many layers of polymorphous cells, among which squamous elements are to be seen. The stroma consists of embryonic connective tissue, which gives a positive mucin reaction in places, and has been differentiated into fibrous tissue in the centres of the papillæ. Owing probably to circulatory disturbances it is often œdematous. Here the cross sections of the papillæ bear a striking superficial resemblance to a hydatidiform mole. No other mesodermal tissue, such as fat, etc., was found.

It appears strange at first sight that the non-malignant epithelium should re-appear in the metastases. It is only found on the ovaries and is limited to the surface. We must assume that the epithelial cells from which the secondary deposits originated were of the cancerous variety. In spite of this they retained their physiological property of covering the surface with a single layer of cells. This character is not unknown in carcinomata, and occasionally gives rise to some difficulty when an opinion as to their malignancy is to be formed.

As it may be suggested that the present case is a primary growth of the ovaries with secondary deposits in the uterus, it may be as well to give the reasons why such a view is untenable. No tumour is present in either ovary which is in any way comparable to an embryoma. Except in embryomata the great variety of connective tissues we have shown to exist does not occur in the metastases of ovarian tumours. The stroma, which is relatively simple in the ovaries, is very complex in the uterine growths, and corresponds in every respect to that of the mixed tumours of this organ. The uterine epithelium readily undergoes a metaplasia into squamous epithelium. I know of but one instance in which this change is said to have taken place in a primary ovarian growth, and that case is open to doubt. It is a cystic carcinoma of the left ovary recorded by Hitschmann (15). A year later the opposite organ was found to be similarly affected. As no mention is made of the state of the uterus and as the description is very short and incomplete, the most probable explanation is that there was a primary carcinoma present in this organ, with secondary deposits in the ovaries.

The small metastases on the peritoneum consist of an undifferentiated epithelium in the shape of solid rods and of tubules, the latter of which often contain small papillomatous projec-

tions. Some epithelial cells are found within the lymphatics, and others infiltrate the stroma. The latter is in every respect identical with the embryonic tissue described above, but does not give a positive mucin reaction (Fig. 9).

The pulmonary deposits contain a stroma that is embryonic, cellular, or fibrous, intermingled with areas of alveolar sarcoma. Epithelium is present as groups of squamous and granular cells, which often occur together.

All the metastases contain the epithelium as well as the stroma of the uterine tumours. Were both kinds of tissue carried to the part, or was the epithelium alone transported? If the latter, then did it exert some formative influence on the connective tissue with which it came into contact, by means of which this was, so to speak, forced to take on the characters of the stroma of the uterine tumours? There is no doubt that epithelium exerts a certain influence on connective tissue. This is purely mechanical and is limited to a process of moulding, as a result of which secondary deposits often present the alveolar, tubular, or villous structure of the primary growth. There is, however, no evidence to show that the stroma of a distant organ can be stimulated to produce tissues as foreign to its nature as are the embryonic and myxomatous stroma, not to mention the alveolar sarcoma.

The view that epithelium and stroma were transplanted is, I believe, the correct one. In an ordinary neoplasm it is only the cells of the parenchyma that are carried away as emboli. They settle in the vessels of distant organs, and give rise to the parenchyma of the metastases. Since they exert the irritative effects of a foreign body on the endothelium, they cause it to proliferate, and to form a stroma for them. Fibroblasts soon wander in, and the stroma may eventually become firm and fibrous. Both these elements enter the circulation in a tumour like the present one, which possesses an epithelial as well as a connective tissue parenchyma. They proliferate together, and give rise to the epithelial and the connective tissue parenchyma of the metastases. In the present instance both are found in the

vessels of the pedicle of E. These metastases differ in this respect from those of embryomata. In these all the constituents of the primary tumour may be found together. Embryomata originate in cells that are comparable, as regards their powers of differentiation, to the ovum. Some of the descendants of these omnipotential cells proliferate in this undifferentiated condition. These, when they reach a distant organ, are therefore able to reproduce all the structures of the primary growth in the secondary deposits.

With the possible exception of those in Douglas' pouch, the metastases have not resulted from dissemination through the rupture of the uterus. This was shut off by adhesions, since there was only a limited local peritonitis.

The Left Round Ligament.

I do not think that the small patch of mucous membrane in this ligament is a secondary deposit, since its epithelium and its stroma differ considerably from those of the nodules under the peritoneum (Fig. 10). The epithelium is very regular, and its nuclei are oval and occupy the same level of the cells. The stroma consists of spindle cells and fibrillæ, and is quite unlike that of any part of the tumours or metastases. It is of the nature of a parovarian remnant, such as not uncommonly gives rise to an adeno-myoma in this situation. One of the earliest cases on record is that of Cullen.[4] It must be remembered that the broad ligament of the same side contains two small cysts, such as are referred to remnants of the Wolffian body by Ballantyne and Williams[1] and all subsequent writers on the subject. I have examined one of these cysts. Except for the flattening and distortion caused by the accumulation of secretion, it is very like the nodule in the round ligament.

Multiplicity of the Uterine Mixed Tumours.

After this discussion of the anatomical features of our specimen, we can turn to the consideration of its mode of origin.

We have seen that the uterus contains two pedunculated polypi and one small finger-shaped one, as well as two sessile tumours, one of which is much larger than the other. We must now attempt to answer the following questions: Are these structures independent of each other, or are the smaller local metastases of the greater?

Ordinary mucous polypi of the uterus are not uncommonly multiple. Those that are not submucous pedunculated fibroids are usually considered to be due to the same cause, namely, some form of chronic endometritis. Piquand[28] has shown that sarcomata of the mucous membrane infiltrate its deeper layers for great distances, and rarely if ever invade the muscle. They often replace the mucosa over the whole of the uterine body. In places where proliferation is excessive folds are produced. Later they become polypoid. These multiple sarcomatous polypi are therefore not real metastases, but connected with one another by less prominent sheets of new growth.

The cases of mixed tumour that have been recorded are too few in number for an opinion as to their usual method of spread within the mucous membrane to be formed. That of Murray and Littler[24] suggests that they behave in the same way as sarcomata. In this connection it should be remembered that tumours D and E were quite superficial. E only infiltrated the muscle to a very slight extent. Hunzicker[16] describes a deposit under the peritoneal coat of the uterus. This is analogous to the distant metastases of our own case, and does not affect the question of the spread within the mucosa.

We have seen that our tumours were not connected by new growth. The appearances around the base of the smallest polypus are opposed to the view that it is a metastasis. They indicate a local conversion of this part of the stroma of the mucous membrane into embryonic tissue. A comparison of the different new growths brings out the fact that they differ considerably as to details of structure. These differences can, I think, be best explained on the assumption of a multi-centric origin. Polypus B is a papillary adenoma. Its stroma is scanty and

shows none of the structures characteristic of the other tumours. C and D resemble the basal parts of E pretty closely, but differ from it in containing very much less sarcomatous tissue (D), or none at all (C). The distal part of E is practically a myxo-chondro-sarcoma. Its growth has been far more rapid than that of the other parts. Here the embryonic tissue has undergone a sarcomatous change, and we should expect the sarcoma to have disseminated rather than the less active parent tissue. But even if it is the embryonic tissue of E that has disseminated, we can hardly account for the abundance of fat in every part of C and D, and for its apparent total absence from the parent tumour. That the former actually can disseminate is proved by the structure of the metastases, in which it is found in a simple form. Here the only differentiation undergone by it is into fibrous tissue and sarcoma, the latter of which occurs only in the lungs. I therefore believe that, if the smaller neoplasms were metastases of the big tumour, their structure would be simpler and that we should not find tissues like fat and skeletal muscle in them; tissues which, if present at all in E, can be so in very small quantities only.

The Tumours are Carcino-Sarcomata.

The view of the multicentric origin of the tumours is strengthened by the behaviour of the epithelium. In every single instance, except in the youngest polypus, it passes through the same stages of malignancy. It is innocent in the superficial, *i.e.*, the youngest parts. It then begins to infiltrate, at first with difficulty in the form of giant cells. The infiltration is best marked in the deepest parts, where contact between epithelium and stroma is most intimate and has existed for the greatest length of time. Areas of true carcinoma occur here (Fig. 5). They are as abundant in D as in E. In C, which is smaller and younger, this stage has not been reached. If D were a metastasis of E, we should expect the carcinomatous changes to be less advanced in it.

The fusion of the epithelial and of the connective tissue elements becomes so intimate that it is always found in the metastases. To this association the name of "carcino- sarcoma" or "sarcoma carcinomatodes" has been given. These terms should be limited to cases in which the two kinds of new growth are situated in, and have originated at, the same spot, and not extended to those that have arisen close together and then invaded each other. The latter were at one time topographically distinct, however closely they may have become connected later, whereas the former are united from the beginning. A good many uterine tumours have been described under these names whose claim to rank as carcino-sarcomata is at least doubtful. Indeed, Forssner,[6] one of the most recent writers on the subject, states that with one possible exception, all the cases recorded point to the conclusion that, in the uterus at any rate, the carcinoma and sarcoma start independently of each other. Genuine carcino-sarcomata have, however, been described in other organs. Two of the most interesting papers on the subject are those of Herxheimer[14] and of Krompecher[19], mainly on account of the diametrically opposite views these writers hold as to their causation. Herxheimer describes an epithelioma of the œsophagus which was imbedded in, and in process of being destroyed by, a mixed celled sarcoma. Krompecher believes that certain basal celled carcinomata of the skin, and the tumours of the parotid and submaxillary glands, are of the nature of carcino-sarcomata.

The malignant change occurs only in the tumours of the present case, the changes in the mucous membrane not passing beyond adenomatous proliferation. Their claim to be genuine carcino-sarcomata are thus established, if we accept this term in its widest sense. That is, if we include carcinomata associated with malignant mixed connective tissue tumours. We must probably place Penkert's[27] case in this group, although his description of the changes undergone by the epithelium is not at all clear.

Is the mixed connective tissue tumour due to some influence exerted on the stroma of the uterus by the actively proliferating epithelium, or did it appear first and cause the latter to proliferate? It is very hard, if not impossible, to decide which answer is the true one. These questions bring us very near to the enigma of the causation of tumours in general. In discussing them we have to leave the realms of solid facts, and embark on the sea of speculation. I can, therefore, but state my own impressions.

The marked proliferation of the epithelium over large areas of the uterus and the pleuricentric origin of the tumours point to the conclusion that it was the former that inaugurated the change. The proliferation reaches its height around the base of the tumours, and here it has adenomatous characters. These changes might be explainable on the assumption that the mucosa was irritated by the neoplasms, and that the irritation was most intense around their bases. But uterine polypi, whether simple or sarcomatous, never give rise to such an excessive and general amount of epithelial proliferation. One finds signs of endometritis around them. The severest reaction I myself have seen was of the nature of a villous endometritis. Carcinomata have, however, been described. Thus, the sarcomatous polypus in one of Forssner's[6] cases was surrounded by an almost complete ring of carcinoma. A general hyperplasia of the uterine epithelium is quite unusual in association with new growths, and cannot, I believe, be placed to their credit. Again, in none of the recorded cases of mixed tumours of the uterus is there mention made of similar changes, so that they cannot be accused of predisposing to a great general proliferative activity on the part of the epithelium. If one may judge from the analogy of normal development, it is the epithelium that leads and the stroma that follows.

I believe, therefore, that the violent activity of the epithelium stimulated the stroma to undergo profound changes in various parts of the uterus. These changes were in the direction of an active dedifferentiation with the assumption of the characters

of embryonic connective tissue. This statement should be understood to refer to normal tissues, since we have evidence that, in blastomata, the epithelium may have a profound influence on the connective tissue and vice versa.

The epithelium assumes carcinomatous characters only when it has been in contact for some time with the tissues of the mixed tumours. It is certain, therefore, that the latter is in some way responsible for this change. When a carcino-sarcoma is studied in animal experiments, it is usually the sarcoma that develops in the stroma of the carcinoma. Haaland[11] has demonstrated the method by which this takes place in the transplanted tumours of mice. There are indications that the reverse process can also take place. Thus, I[25] have found a small carcinoma in the wall of a necrotic sarcoma graft in a rat. I mention these experiments because they can be controlled, and the material examined at any stage. One, therefore, gets a better idea of the sequence of events than is possible from the study of similar tumours in man. The changes are usually far advanced in human material, and the conclusions arrived at depend solely on the opinions held by the pathologist. I believe that this is not so in the present case, and that the evidence is clear that it was the mixed tumour that induced the blastomatous change in the epithelium.

In structure our specimen approaches very closely to certain embryomata. These tumours, when they are typical, contain tissues belonging to the ecto-, the meso-, and the endoderm. Occasionally, however, the first or the last of these layers is not represented. Strictly speaking, the proof should be brought in every case that the epithelium is not mesoblastic, before stating that a specimen is built up of derivatives of two layers. The coelomic epithelium normally differentiates into a large variety of forms, such as squamous epithelium in the vagina, columnar in the uterus, and spheroidal in the ovaries. It must also be remembered that the vaginal mucous membrane, whose differentiation under normal conditions stops short of the formation of horn, is able to exceed it in pathological states,

such as in inflammatory irritation and new growths, and be converted into a keratinising surface. Similar changes occur in the metaplasia of the uterine epithelium. There can be no doubt that there is a fundamental difference between the mesoderm proper or mesothelium, and the mesenchyme of the embryo. The former, from its inception, has all the characters of an epithelium, and, during the course of its subsequent development, gives rise to the epithelial structures of the organs that are formed from it. The mesenchyme is budded off, not only from the mesoderm, but also from the epi- and endoderm, as fusiform and branched cells which follow their parent epithelium and give rise to its stroma. All the connective tissues of the body, with the exception of skeletal muscle, are produced from it. The latter is an epithelium according to its development, and arises from that of the mesoderm, namely, from the muscle plate or myotome. Embryologists are, I believe, in agreement as regards these facts. The time has come for them to be adopted by pathologists.

The present case is, therefore, not an embryoma in the generally accepted sense of the term. It is made up of mesoblastic tissues; the mesenchyme is represented by embryonic and differentiated fibrous tissue, sarcoma, plain muscle, fat, and cartilage, and the mesothelium by skeletal muscle and epithelium. The ultimate origin of the last of these structures is clear, it comes from the lining of the uterine cavity. It is not an original component of the tumours. Its association with the other tissues, however intimate, is purely secondary.

Histogenesis.

It now remains for us to enquire into the way in which the connective tissues, some of which are quite foreign to the uterus, have arisen. Their presence is usually explained by a modification of Cohnheim's theory of displaced embryonic cells. Indeed, the mixed tumours of the uterus are often quoted as one of its strongest supports. It was Wilms[34] to whom, by the way, we owe our present classification and much of our know-

ledge of embryomata, who applied Cohnheim's hypothesis to these tumours. His argument is briefly this: Since skeletal muscle does not arise from plain during normal development, this holds good in pathological conditions. Mixed tumours, therefore, contain elements of the myotome. The other tissues are mesenchymal. The cartilage is a derivative of the sclerotome, a mesenchymal product of the myotome. The parent tissue of such a mixed tumour must, therefore, be equivalent to a primitive mesoderm cell, or to a small group of such cells, at a stage of development prior to the splitting off of the sclerotome from the myotome. Wilms assumes that it actually is such a cell. As no renal elements are present in the tumours, it comes from the part of the body of the embryo behind the kidney anlage. It follows that it is split off from its surroundings at a very early stage of development. It is then carried into the uterus by the backward growth of the Wolffian duct, parts of which are frequently found, as Gartner's duct, in the cervix and vagina down to the level of the hymen. In this manner Wilms explains the mixed tumours of the cervix and vagina. He did not attempt to apply his theory to those of the uterine body. This is, however, easily done on his assumption, since Meyer[21] has found a Gartner's duct in an adult, which ran an abnormal and uninterrupted course in the lateral wall of the uterus, from just below the insertion of the Fallopian tube to the cervix, where it ended in an ampulla.

This theory is a very pretty and ingenious one, as much of it is based on known embryonic rudiments. The only entirely hypothetical assumption it contains is that of dissociated mesoderm cells. This part of the theory cannot be proved any more than it can be disproved. It is only fair to Wilms to state that he brings forward a very pretty piece of collateral evidence in its support. It is afforded by the mixed tumours of the trigone of the bladder. These, one of which has been described by Shattock,[32] have only been found in males. They always surround the ureter at its entrance into the bladder. They are comparable to the mixed tumours of the cervix uteri,

and have reached the base of the bladder by passing along the Wolffian duct and the ureter, which is budded off from the lower end of the duct.

Wilms' hypothesis can, in the way in which I have modified it above, be made to apply to the largest of the tumours of the present case, which springs from the lateral border of the uterus just below the orifice of the Fallopian tube. If we accept the smaller tumours as metastases, they can, of course, be readily explained. If, however, they are independent formations, his explanation fails. Tumour D is at the highest point of the fundus in the exact middle line, and as far away from the tubal angles as circumstances permit. Gartner's duct could not possibly have reached this part of the uterus and have here discharged its burden, even if we are prepared to admit that more than one mesodermal rudiment had been entangled with the Wolffian duct. One explanation only is possible, which is, I admit, quite as hypothetical as that of displaced embryonic tissue. It is as follows :—

Sarcomata are universally admitted to be composed of indifferent embryonic connective tissue cells. This is true, in an even greater degree, of mixed tumours. Now sarcomata are generally believed to owe their origin to indifferent cells. These have either not been used in the building up of the part, in which case they are embryonic in nature, or they have stepped aside, as it were, at some period of extra-uterine life from the paths trodden by their sisters, and remain dormant as useless parasites. This dissociation from the rest of the tissue is, no doubt, often due to separation from mechanical injury, or to the loosening caused by inflammatory exudates. In other cases the cause is not obvious. At a subsequent date these cells are acted on by some quite unknown stimulus, which causes them to proliferate. As they do not functionate and have not got the normal intimate connections with the surrounding cells, they devote the whole of their energy to proliferation. They divide rapidly. Once the habit is induced, division becomes more and more rapid. The cells have no time to differentiate. Actively

growing tissue is younger than the rest of the body. This is shown to be the case by Child[3] in his experiments on the reaction time to poisons. The rejuvenescence is associated with a return of the energy belonging to very young tissue. The cells of a sarcoma are not only undifferentiated, but they fully deserve the name of embryonic cells, since they have regained the characters belonging to them. They correspond to the mesenchyme from which the tissue they originated in was developed.

If the stimulus to growth is exceptionally intense, the reaction to it will be proportionately great. It is conceivable that, in such conditions, the dedifferentiation will be so extreme that it not only reaches the stage of the mesenchyme cells of the part, but passes still further back, even to the stage of the primitive mesoderm. Rejuvenescence in this case keeps pace with the amount of dedifferentiation. The cells thus regain all the characters of mesoderm cells, among others the power of redifferentiating in various directions. They can now form, to limit ourselves to mixed tumours, cells which are analogous to the myotome and to the primitive mesenchyme of the embryo. The former give rise to skeletal muscle, and the latter to all the other members of the connective tissue group. This redifferentiation is most perfect if, once the stage of the mesoderm is regained, the stimulus to growth loses in intensity. The cells then divide less rapidly and have time, between divisions, to begin their redifferentiation.

There is some evidence that analogous changes occur in pathological conditions apart from new growths. Though less profound, they are of considerable value. Such evidence is afforded by the metaplasia of the epithelium of mucous membranes. For a fully differentiated columnar epithelium to be converted into a squamous one, it is necessary that its cells undergo a certain amount of dedifferentiation. A columnar cell with all its characters fully established cannot change into one of the squamous variety, which possesses a totally different set of characters. For this change to occur dedifferentiation must

take place. The cells must revert to a stage in which they can develop into columnar and into squamous epithelium. This they do by rapid division, and lose some of their differentiation every time they divide. Since it is the basal cells of a mucous membrane that normally replace the wear and tear dependent on life, it is they alone that undergo this change. The superficial cells are too rigid to accomplish it. The metamorphosis is more profound and therefore takes place with greater difficulty the farther the tissue is removed from the one whose structure it takes. A lining of squamous epithelium has only once, to my knowledge, been seen in the gall-bladder (Lubarsch[20]). On the other hand, it occurs commonly in the nose and the bronchi in inflammatory conditions. We must suppose that the ability to form squamous epithelium is present in a latent form in such a columnar mucous membrane. The change must be considerable by means of which the cells produce squamous at the expense of their physiological habit of forming columnar epithelium. We have a good example in the mucus secreting squamous cells of the present case that all their original characters of uterine epithelium are not lost as a result of their metaplasia.

Another piece of evidence is found in the changes that occur in the formation of bone in calcified necrotic areas in almost every part of the body. I[26] have recently attempted to explain them in the following manner: The calcified areas are invaded by granulation tissue derived from the surrounding stroma. This is actively growing young tissue. Its fibroblasts, that are among the least differentiated cells in the body, and whose physiological function in these situations it is to develop into fibrous tissue, owing to the abnormal stimulation exerted on them by the saturated solution of lime salts, follow the line of development they would take in the skeleton. Here, as osteoblasts, they lay down bone at the expense of the calcified cartilage. The actual ossification is quite the reverse of pathological; it is only the site that is so.

I had come to the conclusion that, in default of Cohnheim's theory as an explanation of the multiplicity of the mixed tumours in the present case, dedifferentiation with a return to the stage of the primitive mesoderm cell is the only possible one, before I had realised what Hansemann[12] really meant by his theory of Anaplasia. This term is now generally used in a purely morphological sense. If, for instance, the cells of a carcinoma of the intestine have lost their columnar characters, or those of the metastases of an epithelioma produce less horn than the primary growth, they are said to be anaplastic. The term, as originally employed by Hansemann, was meant to apply to a reversion to embryonic characters associated with an increase in the power of independent existence. I have not had an opportunity of seeing his original communication, but gather the impression from criticisms that in it he attempted to find an explanation for the cause of neoplasia. Beneke[2] points out that the only clearly demonstrable difference between the cells of a new growth and those of physiological tissues is a diminution of the functional powers of the former. They have undergone a degeneration and not a return to the embryonic condition. In mixed tumours, for instance, the areas of "embryonic" connective tissue give rise to the cartilage, etc. They grow comparatively slowly. The rapidly proliferating sarcomatous areas, on the other hand, only produce more sarcoma tissue. The "embryonic" tissue must, in his opinion, owe its presence to a displaced rudiment of mesoderm cells, and this has undergone the blastomatous change. In his book on tumours Hansemann[13] protests against the interpretations applied to his statements. The term "anaplasia" was intended merely to give a name to the loss of differentiation and increased powers of independent existence that are in fact found in neoplasms. It was not meant in any way to explain the ætiology of new growths. Because the cells have undergone this change they give rise to a new kind of cell which differs from all those of the body. When it is subjected to the "cancer" stimulus, it responds by boundless proliferation and the production of a malignant new growth.

I cannot agree with Hansemann in this. I believe that the phenomena of dedifferentiation and of rejuvenescence are inherent in all tissues, and have brought forward evidence that I believe to bear on this point.

Conclusions.

Mesodermal mixed tumours of the uterus can be multiple. The smaller are not necessarily local metastases of the largest.

The epithelium of the uterine mucous membrane, which shows signs of a general and excessive physiological proliferation, becomes blastomatous over several of the mixed tumours. It infiltrates their deeper parts in the form of multicentric carcinomata, which blend intimately with their tissues. True carcinosarcomata result.

This union of the epithelium with the parenchyma of the mixed tumours is reproduced in all the metastases.

The multiple mixed tumours cannot be explained on Wilms' modification of Cohnheim's theory, owing chiefly to the situation of one of them at the fundus uteri.

They can be explained on the assumption of a process of dedifferentiation and rejuvenescence of the stroma of the uterine mucosa. It is analogous to metaplasia of epithelium and to heterotopical bone-formation, and has taken place independently at several points.

Until the cause of neoplasia in general shall have been discovered, that of this metamorphosis will remain quite unknown.

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DESCRIPTION OF FIGURES.

Fig. 1.—For full description see text. The uterus is viewed from behind. The lower end of the rectum is turned downwards and the inflamed peritoneum of Douglas' pouch with small nodules of growth is shown. A probe indicates the position of the cervix.

A = granular areas of uterus.
B = adenomatous polypus.
C = larger polypus.
D = triangular tumour of fundus.
E = large tumour.
F = fibroid of fundus with smooth central cavity.

Fig. 2.—A piece of the uterine mucous membrane, whose epithelium has undergone great proliferation with formation of syncytia. The largest of these has dragged the stroma outwards as a small angular elevation. This is the first stage in the formation of papillæ.

Fig. 3.—The edge of the adenomatous proliferation of the uterine epithelium over the pedicle of E. The endometrium, which is bounded by the muscular coat, is atrophied and contains numerous compressed uterine glands. The adenomatous formations consist of dilated tubules lined by columnar epithelium. Irregular papillæ project into their lumina, which contain masses of desquamated epithelial cells in all stages of decomposition.

Fig. 4.—From the surface of polypus C. An area of young squamous epithelium with rounded nuclei is shown. At one end it forms a projection, in which differentiation in the direction of fibrillation and of keratinization has taken place. This abuts on a row of columnar cells, whose nuclei are oval, and whose cytoplasm is dark and granular. The stroma is myxomatous, with slight fibrillation. Its corpuscles are irregular in shape. It contains, in addition to a capillary blood-vessel, an epithelial giant-cell with irregular lobed nuclei, and, in one corner, two epithelial cells that have lost their connection with the surface.

Fig. 5.—From the deep parts of D. The epithelium of the bottom of one of the crypts has invaded the stroma. It has burst through the somewhat fibrous myxomatous tissue that forms a capsule to an oval area of granulation tissue, a young stage in the formation of the sarcoma described in the text. Here it spreads among the loosely arranged cells of the latter and has formed several tubular carcinomatous acini.

Fig. 6.—From tumour D. An acinus lined by columnar epithelium containing numerous typical goblet-cells is shown. Close by there is a tubular syncytium with no traces of cell outlines and with bunches of nuclei at intervals. The stroma varies in form. Around the larger tubule it is cellular. Around the syncytium it is almost homogeneous. In the rest of the drawing it is fibrillated and contains a few fat-cells with crescentic nuclei.

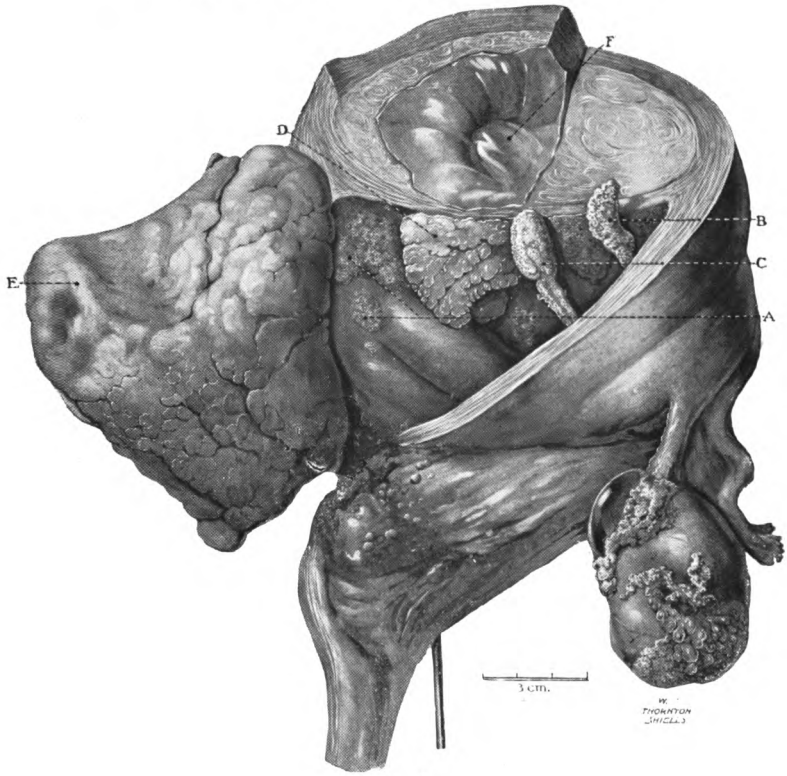
Fig. 7.—A part of a nodule of hyaline cartilage from E. The section has been stained with mucicarmine, which shows the capsules around the cartilage cells as dark rings. At one side of the drawing the hyaline matrix shades off into that of the sarcomatous parenchyma. At the other side the nodule has a sharp border.

Fig. 8.—Numerous elements of skeletal muscle from D. They are imbedded in an almost homogeneous myxomatous tissue, which is slightly condensed to form a kind of perimysium around some of them. The youngest muscle cells are small and spindle shaped. They grow in size and form bands with ribbon-shaped nuclei, as well as multinucleated irregular giant-cells which have undergone a vacuolar degeneration.

Fig. 9.—From one of the peritoneal metastases. The epithelium occurs as carcinomatous alveoli with necrotic centres. The largest of these has invaded a wide lymphatic space, whose endothelial lining is well preserved. The carcinoma is incompletely surrounded by cellular embryonic stroma. This shades off into the subperitoneal connective tissue. The latter is infiltrated with leucocytes, its surface is necrotic, and its capillaries are widely dilated and filled with blood.

Fig. 10.—Represents the Wolffian tubules in the left round ligament. They are surrounded by a fibro-cellular stroma, and are lined by cubical epithelium, which is thrown into folds. A characteristic sharp bend occurs in several of them. The stroma on one side has a well defined border, on the other it passes into the tissue of the ligament, which consists of an areolar framework, imbedded in which there are numerous bundles of plain muscle, a thick walled small artery, and several large veins.

Multiple Mesodermal Mixed Tumours of the Uterus, Associated with Pleuricentric Carcinomata.



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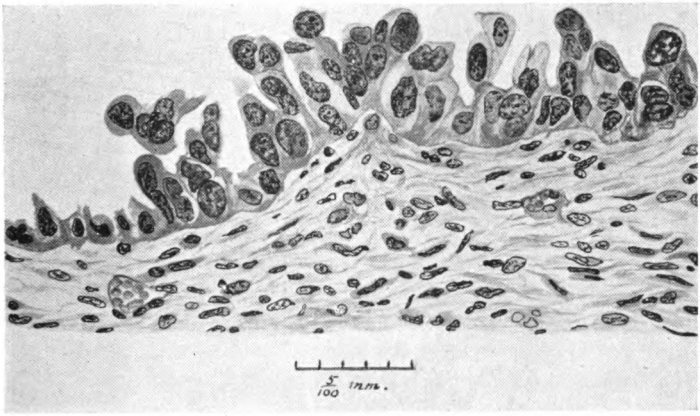
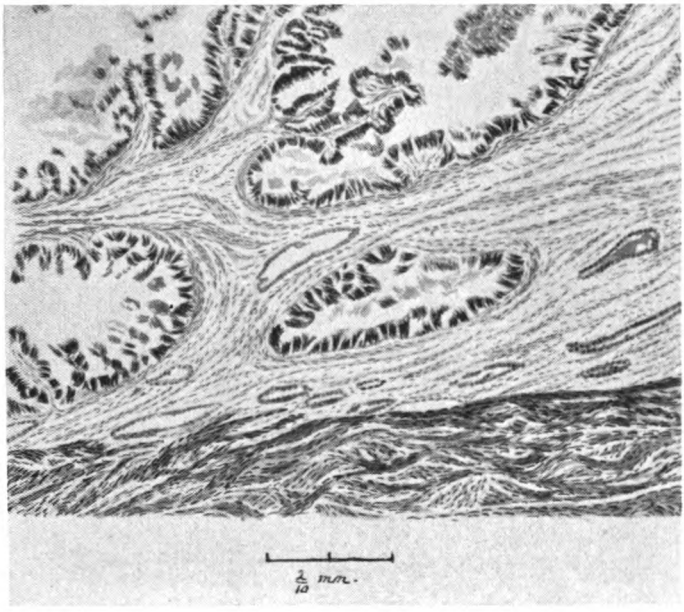


FIG. 2.

Multiple Mesodermal Mixed Tumours of the Uterus, Associated with Pleuricentric Carcinomata.



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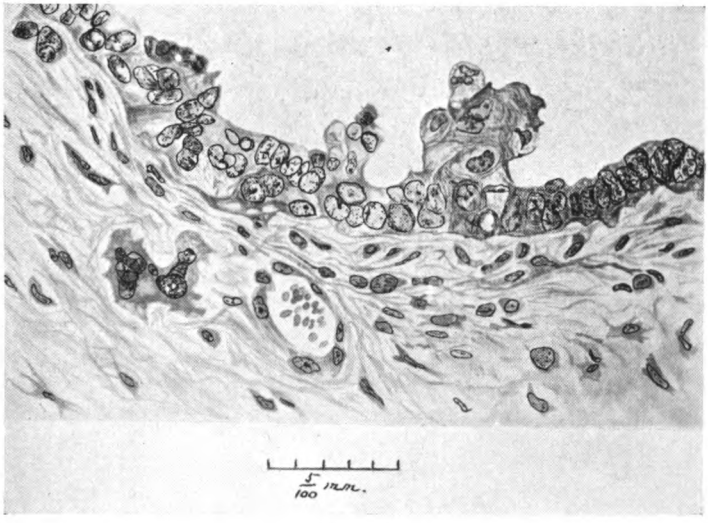

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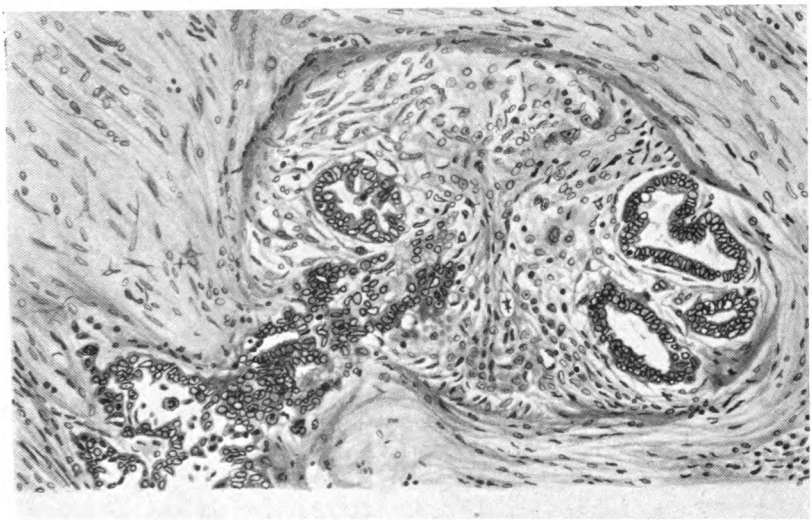

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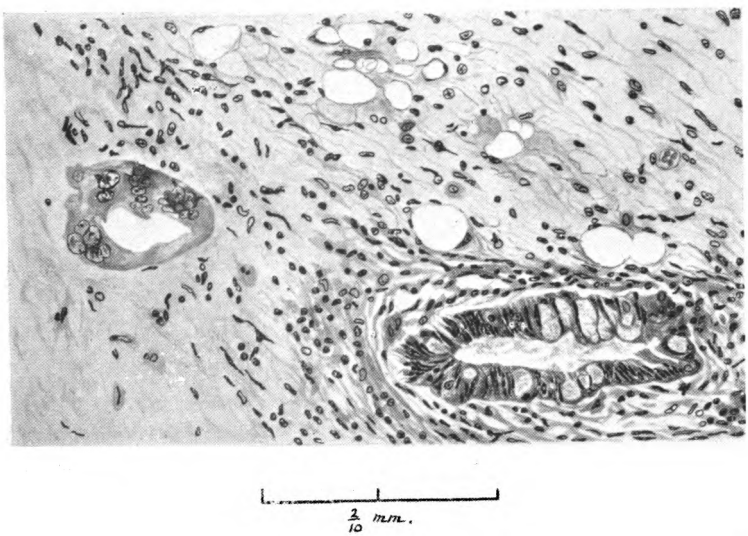

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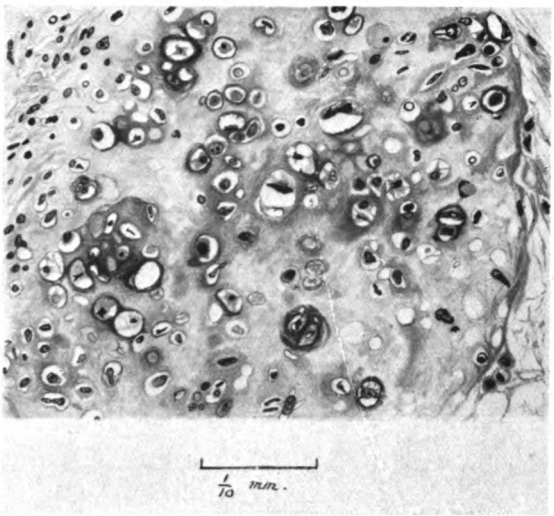

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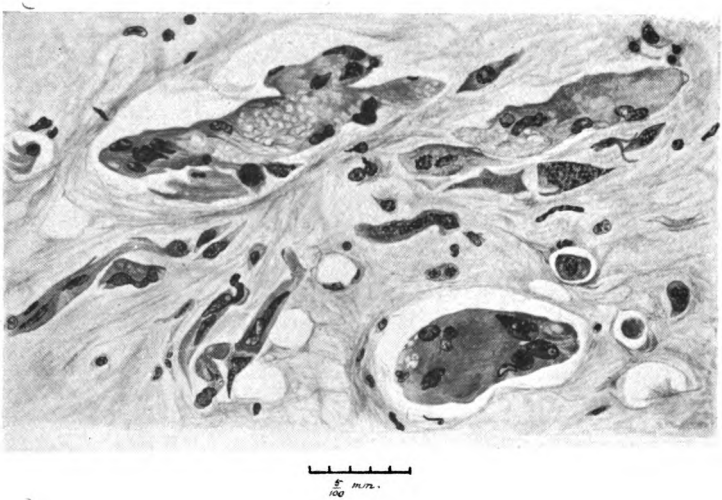

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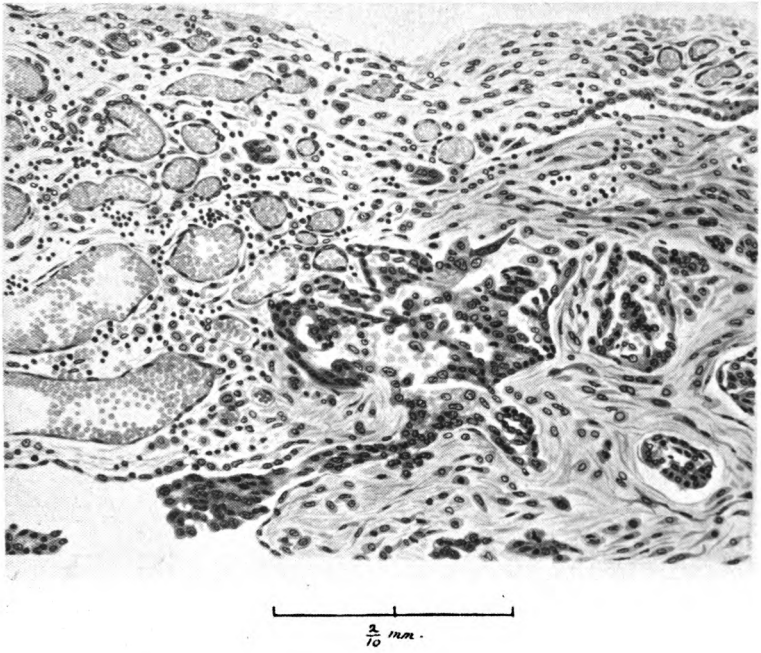

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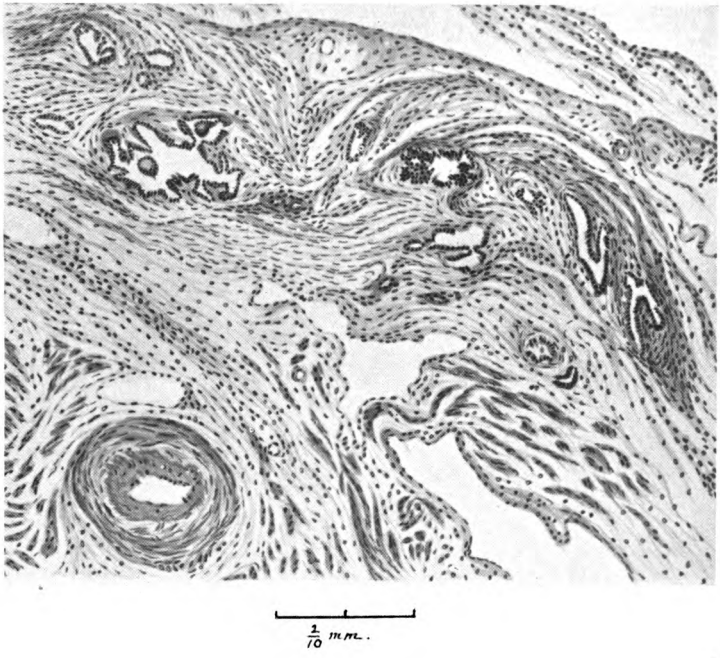

ADENOMA OF THE CHOROID PLEXUS

By

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(From the Pathological Department).

Amongst the more uncommon cerebral tumours are those arising in connection with the choroid plexus. Audry in reporting a case in 1886, collected 25 others from the literature, and a few more have been noted from time to time since the appearance of his paper. They comprise a number of different types of tumour—lipomata, psammomata, fibromata, adenomata, and cysts, together with a few of doubtful histology, but apparently of a malignant nature. They are situated most frequently in the fourth ventricle, and here if they are of sufficient size, whatever their nature, they act mechanically and bring about distension of the ventricles.

The adenomata form the most considerable group and appear to be invariably fatal. Occurring at any age (9 months to 42 years), they produce a variety of cerebral symptoms with failure of sight, hearing, and general intelligence, and loss of muscular power, ending, as a rule, in less than six months from the onset of definite symptoms in coma and death. The histological structure in nearly all cases resembles very closely that of the normal plexus, and in the case here described the microscopical sections might well be taken as those from the plexus of a normal child.

J. C., a girl of 6 months, was admitted to Miriam Ward under the care of Dr. Fawcett on July 17th, 1910, with convulsions. The illness had begun three weeks previously with vomit-

ing and fretfulness, and three days before admission the mother had detected a slight squint. On admission, the head was found to be abnormally large with the anterior fontanelle tense and bulging. The head was retracted, and there was marked internal strabismus. The retraction of the head and rigidity of the limbs grew steadily worse; they were very definitely, though only temporarily, relieved by lumbar puncture, 10 to 20 c.c. of cerebro-spinal fluid being withdrawn daily. Direct microscopical examination of the centrifugalised deposit showed only an occasional lymphocyte, and cultures invariably failed to show any growth of micro-organisms. Great hydrocephalus developed, and the child died on August 17th.

Post-mortem Report.—A very wasted infant. The head was very large, the cranial bones being widely separated and extremely thin. On opening the cranial cavity 820 c.c. of clear fluid were obtained. The brain was very soft and even with the greatest care it was impossible to remove it without a considerable amount of damage. The pia mater was everywhere thin and translucent, and there was no evidence of any meningitis either at the base or over the cortex. The lateral ventricles were enormously dilated, and so great was the consequent thinning of the cerebral cortex that nowhere was the brain substance forming the roof and outer wall of the ventricles more than a quarter of an inch in thickness. Both ventricles were equally dilated. At the postero-internal angle of the right lateral ventricle just at the junction of the body of the ventricle with the posterior cornu was situated a rounded tumour measuring $4 \times 3\frac{1}{2} \times 3\frac{1}{2}$ c.m., reddish-purple in colour, velvety in appearance, and firm to the touch. It was attached to the choroid plexus, but nowhere invaded the cerebral substance. Emerging from the centre of its upper surface was a much distended vein 5 m.m. in diameter which ran forwards and inwards to the middle line. The tumour was firmly anchored in position by its attachment to the plexus, and so far as could be judged it did not seem possible that its position could have been affected by any alteration in the position of the patient during life.

Histological examination.—Several pieces of the tumour were taken for microscopical examination, but all showed the same picture. The whole tumour was composed of a number of papillomatous processes consisting of a central capillary with only a very delicate endothelial wall covered with a single layer of cubical or short columnar epithelium. In only a few of the processes was there any definite amount of connective tissue separating the epithelium from the central capillary; no concentric calcareous bodies, such as are seen in the normal adult plexus, were found anywhere in the tumour. It therefore resembled very closely the normal histological picture of a choroid plexus of the infant type. Death had taken place several hours before the autopsy, so that it was not possible to obtain any histological evidence as to the secretory activity of the epithelial cells.

Quite apart from any interest that may attach to this case from the comparative rarity of such tumours there is a further point worth a little consideration, viz., the way in which the hydrocephalus was produced. Dr. Mott has noted a case of a small tumour of the plexus in which he was able to demonstrate that in certain positions of the patient the tumour fell forward and, acting as a ball valve, caused an intermittent obstruction to the flow of fluid from the ventricles. In the present case, however, the anatomical arrangement precluded any such possibility, and it seems at least very probable that the hydrocephalus was produced by the secretion of the cells of the tumour. Such a suggestion does not seem to have been put forward before, and some support may be found for it in a consideration of the conditions of the previously recorded cases.

Amongst 14 cases of adenoma of which the details are available, 10 were situated in the fourth ventricle; in the only 7 of these in which the condition of the ventricles is mentioned, there was in all a considerable excess of fluid, producing frequently very great distension. In these cases, however, it is clear that we cannot exclude the mechanical factor, and, indeed, other tumours of completely different structure, such as lipomata and cysts have produced an equal degree of hydrocephalus.

I can only find records of four cases of adenoma of the choroid plexus situated in the lateral ventricles, and a short summary of the pathological condition in these is given here; three were collected in Audry's paper, and one has since been described by Brüchanow. In all of them the hydrocephalic condition was of considerable degree.

Audry.—A tumour of the size of a small nut attached to the choroid plexus in the left lateral ventricle; it was freely mobile, of slightly irregular surface, and of the colour of the cerebral tissue; histologically it was a papilloma resembling the normal plexus.

Demange.—A pedunculated tumour in the posterior cornu of the left lateral ventricle attached to the choroid plexus, about the size of a walnut; the histological structure was that of the normal plexus.

Chambard (quoted from Audry).—A tumour situated at the junction of the body of the lateral ventricle and the posterior cornu; of the size of a tangerine orange, weighing 70 grammes, irregularly lobulated, covered with strands of connective tissue in which were recognisable traces of the choroid plexus. Chambard himself calls this tumour an epithelial sarcoma, but Audry classes it amongst the epithelial tumours, and it appears clearly to be an adenoma.

Brüchanow.—A large rounded tumour 5 c.m. in diameter attached to the choroid plexus of the left lateral ventricle. Histologically it is described as hyperplasia of the plexus.

All these tumours were situated at the posterior end of the ventricle arising from the globus, and it is difficult to see how any of them can have had any direct mechanical action in obstructing the flow of fluid from the ventricle. Although it seems to have been assumed by previous writers that the hydrocephalus was due to mechanical factors, they have ascribed it not to direct interference with the outflow of fluid, but to disturbances in the circulation through the plexus and consequent œdema of the cerebral tissues and extravasation of fluid into the ventricles. If this were the true explanation, distension of

the ventricles with fluid should also accompany tumours other than adenomata; such tumours are apparently very rare, and I have not been able to find any of importance other than those recorded in Audry's paper. Amongst these, however, there are four of considerable size, and none of them were associated with any excess of fluid.

Bonnet described a large bony tumour, roughly the size of an astragalus, completely filling the lateral ventricle and intimately connected with the choroid plexus in which it appeared to have had its origin.

Cayley and Brown record a cyst the size of a duck's egg arising from the choroid plexus, filling the lateral ventricle and penetrating the brain substance so as nearly to reach the dura mater. The cyst itself was filled with clear fluid, but there was no excess of fluid in the ventricle.

Obersteiner found a small lipoma $\frac{1}{2}$ c.m. in diameter which produced no effects pathologically or clinically.

Beigel described a case where the plexus on both sides contained a number of small cysts, and at their anterior extremities, situated symmetrically just at the foramina of Munro, a cyst of the size of a small nut.

Whether we consider these tumours from the point of view of their relationship to the choroid plexus or from their situation in the ventricle, they seem at least as favourably placed for producing disturbances in the circulation as do the adenomata; yet one group was invariably associated with great hydrocephalus, the other not once. An interesting case was reported by Saxer of an adenoma of the lateral ventricle arising from the ependyma of the ventricle and in no way connected with the choroid plexus; here there was only a small amount of fluid in the cavity. Whatever views may be taken as to the relationship of the epithelium of the choroid plexus and the ependyma of the ventricle, it is clear that tumours derived from these two sources might well be functionally different, and even if we allow that an adenoma may have the power of secreting the fluid necessary to produce hydrocephalus, there is no reason to suppose that all adenomata would do so.

However the hydrocephalus may be produced, it is certainly the chief factor in producing the main symptoms. In the present case the child was thought to be dying of tubercular meningitis. In those cases where the tumour is in the fourth ventricle there may be additional localising signs such as glycosuria. In a case reported by Vigouroux a fistula was established between the ventricle and the nasal cavity, and there was a daily flow of 800 c.c. of cerebro-spinal fluid from the nose. During the last three years of life this passage frequently became blocked, and at such times there was violent headache followed by epileptiform attacks which continued until the pressure of the fluid became sufficiently great to break down the obstruction and recanalise the fistula.

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THE IMPORTANCE OF TEMPERATURE IN RELATION TO ANÆSTHESIA.*

By

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AND

F. E. SHIPWAY, M.A., M.D.

The influence of temperature upon the exchange of material in animals has been long recognised by physiologists, and during experiments involving operations under anæsthesia they have been accustomed to take precautions to maintain the bodily heat. Surgeons following the teaching of physiology have adopted similar precautions. The custom is well established, even if the reasons have not been fully appreciated. In this paper, which is based both upon physiological experiments and clinical experience, we propose to consider the influence of temperature during anæsthesia.

The temperature of the body in warm-blooded animals is an expression of the metabolism or exchange of material; in other words it represents the oxidation or combustion which occurs in the tissues. The relationship between the temperature of the deep parts, such as the rectum, the closed axilla or groin, and superficial parts, such as the skin, is an expression of the efficiency of the nervous control exercised upon the production and loss of heat. The activity of a tissue is accompanied by an in-

*For a preliminary communication upon the results of this work see Ref. 2. The special thermometers were supplied from grants from the Royal Society and the British Medical Association.

creased temperature in the part, and, therefore, it is possible from a study of such changes to obtain indications for the proper use of heat and cold as therapeutic agents.

It is necessary as a preliminary to insist upon the difference between the effect of heat and cold upon a healthy man with full control over the production of heat in his tissues and the loss of heat through the blood exposed in the vessels of his skin and the anæsthetised subject, who, as the result of the anæsthetic, has lost the normal sensations of heat and cold and the control over both the production and loss of heat. The former on exposure to cold increases the production of heat in his body and diminishes the loss by contracting his cutaneous vessels; the latter does not react in this way, for he is more or less paralysed by the anæsthetic.

The healthy man in a condition of profound rest, such as a deep sleep, is not comparable to an anæsthetised subject, although the comparison between surgical anæsthesia and sleep has often been and is still made. During sleep the muscles are in a condition of tone and are not paralysed, and there are responses to tactile and thermal stimuli; on the other hand, the excitability of the nervous system is undoubtedly lowered during sleep, the metabolism is diminished, and the temperature falls; indeed, there is evidence that the regulation of the production and loss of heat is imperfect. In surgical anæsthesia the object is to produce paralysis, and such a condition must involve changes in all the systems of the body. The body works as a whole, and a general anæsthetic, as opposed to a local anæsthetic, will have a profound effect; the paralysed muscles will produce less carbon dioxide and less heat, the nervous system will not respond readily to external stimuli, the regulation of temperature will be abolished, and the chemical changes in the cells of the body will follow the ordinary law, that is, will rise and fall with the temperature. The respiration and circulation have been regarded as the most important systems to consider during anæsthesia, and temperature has an important effect on both. A rise of temperature increases the excitability of the respiratory centre and quickens the heart beat.

After this introduction it will be well to consider in more detail the chief points and to illustrate them by the results of experiments upon animals and observations upon man.

In the first place, anæsthesia reduces the output of carbon dioxide and the intake of oxygen; in small mammals, such as the mouse, the reduction may be as great as one-half the normal value, as shown by the following examples :—[3]

14/iv./93.—Black and white mouse No. 1 in the ventilated chamber, water bath=10·5° C. for 8 minutes before the first period. Consecutive periods of 20 minutes.

Output of carbon dioxide in decimgrms.	Temperature of water bath, C.	Remarks.
931	10·5°	Normal.
482	11	Anæsthetised by ether.

7/v./93.—Black and white mouse No. 1 in the ventilated chamber, water bath = 14° C. for 5 minutes before the first period. Consecutive periods of 30 minutes.

Output of carbon dioxide in decimgrms.	Temperature of water bath, C.	Remarks.
1216	14°	Normal.
629	14·25°	Anæsthetised by ether.

In larger mammals, such as the rabbit, experiments show that the reduction in the respiratory exchange is much less; this is related, as will be mentioned later, to the slower cooling of the animal. It would follow as a result of the reduction of metabolism that there should be a fall in the temperature of the body, unless the loss of heat were reduced. It is, indeed, well known that the internal temperature of the body may reach a very low level if no precautions are taken to diminish

the loss of heat. During anæsthesia very low records would not be found in man except in the case of accidents or suicidal attempts, but in drunkards exposed to cold, rectal temperatures as low as 75·2° F. (24° C.) have been observed, and the patients have recovered under careful treatment and nursing. In animals it is well known that a considerable fall in the rectal temperature may occur during anæsthesia. The following are examples from our observations :—

Animal.	Rectal Temperature.		Method and Duration of Anæsthesia.	Temperature of air of room.
	Before Anæsthesia.	After Anæsthesia.		
Rabbit	38·5°C.	34·5°C. 32·0°	Open ether for 29 minutes followed by warm ether for 29 mnutes.	14°C.
do.	38·25	35·0° 31·5°	Warm ether for 29 minutes followed by open ether for 28 minutes.	14·5°

The contrast in the response of the normal animal and of the same animal under anæsthesia to changes of external temperature is very definite, and is shown by the following examples :—[3]

Black and white mouse in the ventilated chamber, water bath =28° C. for 10 minutes before the first period. Consecutive periods of 10 minutes.

Output of carbon dioxide in decimgrms.	Temperature of water bath, C.	Remarks.
202	30°	Mouse quiet.
212	29	do. washing itself.
185	27·75	do. active.
345	13·5	do. very active, trying to get out.
350	13·75	do. do.
365	14	do. do.

Black and white mouse A in the ventilated chamber, water bath=25° C. for 50 minutes before the first period. Consecutive periods of 15 minutes.

Output of carbon dioxide in decimgrms.	Temperature of water bath, C.	Remarks.
·437	25	Mouse sent under ether.
392	25	Mouse under ether.
290	13·5	do. do.
308	13·5	do. do.
185	13·5	do. do.

The mouse was fully under ether when taken out of the respiration chamber. It took about 15 minutes to recover from the anæsthetic.

The normal animal responds to external cold by muscular activity which increases the production of heat and carbon dioxide; within 10 minutes of a change of external temperature from 27° to 13° C. the discharge of carbon dioxide was almost doubled. On the contrary, a similar fall of external temperature produced the opposite effect in the anæsthetised animal.

In discussions upon the influence of warmth during anæsthesia, there has been in many cases a misunderstanding of the complexity of the problem. The important factor is not the actual amount of heat which may be communicated to the patient, but the effect of a high external temperature upon the production of heat in the body.

Anæsthesia must be considered in relation to its intensity and duration. Light anæsthesia will not produce such profound effects, for the paralysis of muscles and the regulation of metabolism are in proportion to the depth of anæsthesia. The duration of the anæsthesia is another factor which complicates the results. A big animal or a patient starts with a certain reserve of heat, and the temperature of the mass of the body is not easily altered in a short time. This latency may be well seen

after the operation is over, the lowest record may then be obtained. In the same way it is difficult to raise rapidly the temperature of the body by external sources of heat. Thus it follows that the anæsthetist should pay attention to the temperature before, during, and after an operation. It is obvious also that the duration and extent of the exposure of the skin and the viscera during operations must be taken into account.

The custom of giving morphia before operations is now so general that it should receive some attention here. The small doses given in civilian practice do not intensify to any great extent the effect of the anæsthetic upon the temperature, but there is evidence that in the Navy and Army the drug has been administered in doses so large as to produce a considerable fall of temperature, especially when the patient has been exposed to cold.

The observations which form the subject of this paper were made (chiefly by F. E. S.) upon patients in the ordinary surgical practice of Guy's Hospital. The thanks of the authors are due to the surgeons for the facilities they have afforded and the kind interest they have taken in the work, and also to the sisters and nurses for valuable assistance.

The records were made before, during, and after anæsthesia (conducted by F. E. S.), and relate to both surface and deep temperatures. The former were determined by a mercurial thermometer with a flat bulb, the latter by a clinical thermometer in the rectum, for it has been shown that the mouth does not represent the real internal temperature of the body. For examples the following may be given :—

Case.	Disease.	Temperature of mouth.	Temperature of rectum.
15	Acute appendicitis and general peritonitis.	95·5°	100·8°
22	Strangulated inguinal hernia.	96·8°	99·6°
66	Malignant disease.	99°	100·4°
64	Appendicitis.	99·2°	100·4°

The operations were almost invariably performed in the afternoon between 2 p.m. and 6 p.m., and on this account variations in the temperature of the body due to the time of day are excluded. The method of "open ether" used is that in which ether is dropped continuously on to some fabric spread over a Schimmelbusch mask, which is so closely applied to the face that the whole of the respiratory current passes through the fabric; when "warm ether" is given, the end of the tube from the apparatus[1] (Shipway's) is placed under the mask and ether vapour pumped in at each inspiration. With this method the temperature under the mask through which the patient is breathing varies, as the tables show, from 48·2° to 86·9° with "open ether," and 87·8° to 93·2° with "warm ether." There is little doubt that with minimum and maximum thermometers a greater range would be recorded in the case of "open ether," but from a practical standpoint the reading of an ordinary thermometer is the most important. The "temperature in the airway" (see tables) represents the observations made upon the air in the mouth respired through a Hewitt's airway.

In most cases the administration of the anæsthetic was preceded by a subcutaneous injection of 1/6th grain of morphia and 1/100th grain of atropine, or of atropine alone. Induction was usually carried out by C.E. mixture (C_2E_3) upon an open mask.

The cases have been arranged according to three factors: method of anæsthesia, age of patient, and temperature of the operating theatre. Group I. relates to ages between 16 and 66 years, Group II. to ages between four weeks and 15 years.

The Groups are subdivided into Section A for the range of external temperature between 67·1° and 75·2° (19·5° and 24°C.), and Section B for the range 75·2° and 85·28° (24° and 29·6°C.); these sections are in turn divided into two Parts (i.) Warm Ether and (ii.) Open Ether. (See Tables 1 to 8.)

In considering the results of these observations it is necessary, as far as possible, to make allowance for the influence of

the various accessory factors, which might complicate the effects, such as the severity and duration of the operation, the exposure of viscera, and the condition of the patient. This can be done in some measure by taking the average of the results and at the same time giving the range of the variations in the deep and surface temperature. The next table was constructed on that plan. (See Table 9.)

An examination of the table shows that there is a definite influence exerted by the warm ether, when the other conditions are as far as possible comparable. The contrast between anæsthesia by "warm ether" and "open ether" is more clearly shown when the results are expressed in percentages, as in the following table :—

Group.	Section	Age of patients.	Temp. of air of operation theatre.	Rectal temperature.			Surface temperature of forearm.				Surface temperature of thigh.				Method of Anæsthesia.
				Rise.	Fall.	No change.	Rise.	Fall.	No change.	No Record.	Rise.	Fall.	No change.	No Record.	
I.	A (i.)	16 to 66 years.	67·1 to 75·2°	18·2	72·7	9·1	68·2	9·1	18·2	4·5	31·8	50·0	13·6	4·6	Warm ether.
I.	A (ii.)	ditto	ditto	4·0	96·0	—	76·0	16·0	4·0	4·0	20·0	68·0	8·0	4·0	Open ether.
I.	B (i.)	ditto	75·2 to 85·28°	26·7	46·6	26·7	80·0	6·6	6·7	6·7	46·6	40·0	6·7	6·7	Warm ether.
I.	B (ii.)	ditto	ditto	18·8	75·0	6·2	81·2	18·8	—	—	31·3	62·5	6·2	—	Open ether.
II.	A (i.)	4 weeks to 15 yrs.	68 to 75·2°	43·7	31·3	25·0	81·2	6·3	—	12·5	50·0	25·0	—	25·0	Warm ether.
II.	A (ii.)	ditto	ditto	15·8	79·0	5·2	84·2	5·3	10·5	—	26·3	52·7	10·5	10·5	Open ether.
II.	B (i.)	ditto	75·2 to 85·1°	54·5	27·3	18·2	81·8	—	—	18·2	63·6	18·2	—	18·2	Warm ether.
II.	B (ii.)	ditto	ditto	28·6	57·1	14·3	85·7	14·3	—	—	—	71·4	28·6	—	Open ether.
All	All	All	All	35·8	44·5	19·8	77·8	7·3	12·4	—	48·0	33·3	10·1	—	Warm ether. 64 cases.
All	All	All	All	16·6	76·8	8·6	81·8	13·6	7·2	—	25·9	63·6	13·3	—	Open ether. 67 cases.

It will be observed that the number of cases of a rise in the surface temperature of the forearm during anæsthesia is similar throughout all the sections, but there are more cases of a fall of temperature with the "open ether" as well as fewer cases of no change in temperature. In the case of the surface temperature of the thigh the advantage of the "warm ether" in maintaining the temperature of the body is definite. There may be several explanations of the contrast between the changes in the surface temperatures of the forearm and thigh during the two methods of anæsthesia; it might be due to the more complete covering of the arms and their close approximation to the body; on the other hand there is the possibility of causes connected with the circulation, either the shorter circuit in the forearm or differences in vaso-motor control over the upper and lower limbs. Since no special observations have been made to test these possible explanations, it is unnecessary to say more.

As regards the influence of atropine, there is some evidence of vaso-dilator action upon the skin, as shown in the following examples. The combined action of morphia and atropine shows no more definite effect upon the temperature as far as our observations go.

Case.	Temperature of skin.				Temperature of Rectum.		Interval.	Injection.
	Forearm.		Thigh.					
	Before.	After.	Before.	After.	Before.	After.		
68	84·2°	89·6°	—	—	100·2°	—	60 minutes.	$\frac{1}{150}$ gr. of atropine.
71	95·0	96·08	96·35	96·8	99·4	99·4	100 "	$\frac{1}{100}$ " "
34b	95·0	95·18	95·9	97·25	99·2	99·2	35 "	$\frac{1}{100}$ " "
30b	92·12	93·74	95·45	95·45	99·6	99·2	60 "	$\frac{1}{6}$ gr. morphia. $\frac{1}{100}$ gr. of atropine.
36b	93·2	93·65	96·1	97·25	100	100	30 "	" "

The few cases of anæsthesia with chloroform or chloroform and ether have been collected in a separate table and the cases

of patients with a pyrexial temperature in a further table; in the latter there are seven cases of "warm ether" and two of "open ether" anæsthesia. The details are given, but the number of cases is too small to justify conclusions being drawn. (See Tables 10 and 11.)

An examination of all the records shows no higher rise of rectal temperature during the anæsthesia with "warm ether" than 2·8° in case 74, a child with an initial temperature of 98·6°, one of 101·4° after the operation, 99·8° two hours later, and 99·2° four hours later. Deep anæsthesia will paralyse the regulation of the temperature of the body, and it is possible, as experiments on animals prove, to produce hyperthermia even of a fatal nature by excessive external heat. In man, however, these conditions would very rarely, if ever, arise, for the exposure of the body during an operation and the vaso-dilator effect of the anæsthetic would prevent any serious rise of the internal temperature. It should be stated further that in none of the cases given in this paper were any untoward effects of the anæsthetic observed; as a general rule the aim has been as light an anæsthesia as was consistent with the requirements of the operation.

CONCLUSIONS.

A comparison of 64 cases of anæsthesia with "warm ether" and 67 cases with "open ether" proves that the former method maintains the temperature of the body in a far more efficient manner than the ordinary means of preventing loss of heat when the latter method is used. Thus, with "warm ether" the respective percentages of rise, fall, and no change of rectal temperature were 35·8, 44·5, and 19·8 as against 16·6, 76·8, and 8·6 with "open ether."

A detailed analysis of the cases arranged according to age and temperature of the air of the operation theatre shows that the advantage in each section lies with the "warm ether" method.

The great practical advantage of the "warm ether" is that it enables the surgeon to operate in a cooler theatre; the patient can be kept warm without exposing the staff to the depressing effect of high temperatures. Apart from diminished efficiency and endurance, a warm and moist atmosphere introduces the danger of the sweat of the surgeon and his assistants undoing the elaborate precautions taken to preserve aseptic conditions.

The observations upon man agree with the physiological experiments upon animals and confirm the clinical conclusion that the vitality and resistance of the patient are better maintained under "warm ether." This advantage in the case of long operations or operation upon a patient possessing a low resistance may make all the difference between success and failure.

REFERENCES.

1. F. E. Shipway, Lancet, January 8th, 1916, p. 70.
2. M. S. Pembrey and F. E. Shipway, Proc. Roy. Soc. Med., ix., 1916, No. 7.
3. M. S. Pembrey, Proc. Physiol. Journ. Physiol. xvii., 1895, p. iv.; xv., 1894, p. 401.

1 67·1°—75·2°.

o. of Case.	Sex.	Age.	of of ıtre.	T. of Ether Vapour.	Duration of Anæsthesia.	Duration of Ether Anæsthesia.	T. of Air under Mask.	T. of Air in Airway.	REMARKS.
24	F	22	2·5	84	48	43	91·4	95·9	R. T. 99·8° at 6.45 p.m., 2 hours after operation, 100 4° at 8.45, 100·8° at 12.45 a.m.
28	M	17	3·4	88·3	34	29	89·6	90·5	R. T. 100° at 7 p.m., 4 hours after operation, 98·8° at 10 p.m.
39	M	32	1·6	86·9	58	53	89·6	—	R. T. 98·8° at 7 p.m., 1½ hours after operation.
40	F	35	1·6	—	31	27	—	—	R. T. 98·6° at 6 p.m., 2 hours after operation.
43b	F	32	3·4	91·4	36	32	89·6	—	R. T. 99·2° at 5.30 p.m., 2
31b	F	21	72·05	—	32	32	82·85	—	
36b	M	45	68·45	—	48	48	—	—	Sweating on arms and head.
40b	F	38	71·15	—	23	22	—	—	
41b	M	43	69·8	—	18	16	—	—	
45b	F	20	74·3	—	30	30	—	—	
47b	F	24	68	—	34	32	—	—	
50b	F	20	68·9	—	41	41	75·2	—	
55b	M	57	67·1	—	52	52	—	—	
57b	M	29	68·9	—	27	27	—	—	
61b	M	47	73·4	—	37	35	—	—	
69b	M	37	72·5	—	47	32	—	—	
70b	F	46	72·05	—	53	50	—	—	
71b	F	49	70·25	—	43	43	—	—	
92b	M	45	70·7	—	68	66	—	—	
93b	F	44	68·9	—	53	52	—	—	Anæmic. Sweating on head and neck.

The great practical advantage of the "warm ether" is that it enables the surgeon to operate in a cooler theatre; the patient can be kept warm without exposing the staff to the depressing effect of high temperatures. Apart from diminished efficiency and endurance, a warm and moist atmosphere introduces the danger of the sweat of the surgeon and his assistants undoing the elaborate precautions taken to preserve aseptic conditions.

The observations upon man agree with the physiological experiments upon animals and confirm the clinical conclusion that the vitality and resistance of the patient are better maintained under "warm ether." This advantage in the case of long operations or operation upon a patient possessing a low resistance may make all the difference between success and failure.

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3. M. S. Pembrey, Proc. Physiol. Journ. Physiol. xvii., 1895, p. iv.; xv., 1894, p. 401.

1 67·1°—75·2°.

o. of Case.	Sex.	Age.	of of ture.	T. of Ether Vapour.	Duration of Anæsthesia.	Duration of Ether Anæsthesia.	T. of Air under Mask.	T. of Air in Airway.	REMARKS.
24	F	22	2·5	84	48	43	91·4	95·9	R. T. 99·8° at 6.45 p.m., 2 hours after operation, 100 4° at 8.45, 100·8° at 12.45 a.m.
28	M	17	3·4	88·3	34	29	89·6	90·5	R. T. 100° at 7 p.m., 4 hours after operation, 98·8° at 10 p.m.
39	M	32	1·6	86·9	58	53	89·6	—	R. T. 98·8° at 7 p.m., 1½ hours after operation.
40	F	35	1·6	—	31	27	—	—	R. T. 98·6° at 6 p.m., 2 hours after operation.
13b	F	52	3·4	91·4	36	32	89·6	—	R. T. 99·2° at 5.30 p.m., 2
31b	F	21	72·05	—	32	32	82·85	—	
36b	M	45	68·45	—	48	48	—	—	Sweating on arms and head.
40b	F	38	71·15	—	23	22	—	—	
41b	M	43	69·8	—	18	16	—	—	
45b	F	20	74·3	—	30	30	—	—	
47b	F	24	68	—	34	32	—	—	
50b	F	20	68·9	—	41	41	75·2	—	
55b	M	57	67·1	—	52	52	—	—	
57b	M	29	68·9	—	27	27	—	—	
61b	M	47	73·4	—	37	35	—	—	
69b	M	37	72·5	—	47	32	—	—	
70b	F	46	72·05	—	53	50	—	—	
71b	F	49	70·25	—	43	43	—	—	
92b	M	45	70·7	—	68	66	—	—	
93b	F	44	68·9	—	53	52	—	—	Anæmic. Sweating on head and neck.

3 .ir 75·2°—85·28°.

o. of Case.	T. of Air of Theatre.	T. of Ether Vapour.	Duration of Anæsthesia.	Duration of Ether Anæsthesia.	T. of Air under Mask.	T. of Air in Airway.	REMARKS.
37	78·8	93·2 to 90·5	114	100	89·6	—	Saline infusion at 99·5°, 2 pints subcutaneously.
49	78·35	91·4	39	36	—	—	R. T. = 98·6 at 6 p.m., 2 hours after operation
50	77·9	90·5	32	27	—	—	
51	77	93·2 to 90·5	92	89	—	—	
52	77	93·2	70	67	90·5	—	Emaciated, in bed 6 weeks previous to operation.
67							

Case	heatre.	Vapour.	Dur Ana	Du Eth the	Mask.	Airway.	
26	73·4	86	58	48	—	—	R. T. = 99·2° at 7 p.m., 2¼ hours after operation; 100·4° at 2 a.m. and 100·4° at 6 a.m.
33	72·95	89·6	27	22	89·6	90·05	Thigh uncovered during dressing before temp. taken. R. T. = 99° at 5 p.m., 2¼ hours after operation, and 100° at 7 p.m.
§34	71·15	86	27	25	—	—	Premature child. *Costal margin.
36	72·5	88·7	23	20	87·8	—	†Calf. R.T. = 99° 3 hours after operation. Temp. costal margin. before anæsthesia ... 95·9° after „ ... 96·8°
	70·7	89·6	15	13	—	—	
63	74·48	91·4	65	62	—	—	R. T. = 99·8 at 5·30 p.m., 2¼ hours after operation and 99·2° at 7.30 p.m.
74	75·2	—	32	29	90·5	—	
88	73·4	86	22	19	—	—	*Taken 25 minutes before surface readings
89	74·3	84·2	23	20	—	—	
90	73·4	91·4	31	29	—	—	
29	68·9	89·6	53	50	—	—	Intussusception.
4	71·6	91·4	21	17	—	—	
5	69·8	91·4	39	35	—	—	
5	72·5	91·4	24	21	—	—	Slight general sweating.
6	75·2	93·2	25	25	—	—	General condition very poor.
7	71·15	94·1	22	17	—	—	*Costal margin.

9 week later.

6 f Air 68°—75·2°.

8 of Air 75·2°—85·1°.

o. of Case.	Sex.	Age	T. of Air of Theatre.	T. of Ether Vapour.	Duration of Anæsthesia.	Duration of Ether Anæsthesia.	T. of Air under Mask.	T. of Air in Airway.	REMARKS.
82	M	5	85·1	—	23	21	—	—	
5b	F	7	76·55	—	15	13	—	—	For psoas abscess. Cf. No. 3b in Group II, Section A (ii.)
32b	M	4½	77·45	—	32	30	—	—	Slight sweating on head, chest and arms.
78b	M	9½	78·8	—	34	32	—	—	
81b	M	13	77·9	—	28	28	—	—	Sweating on arms and head.
84b	M	6	77·9	—	22	20	—	—	
88b	F	9	77	—	25	22	—	—	Delicate child, wrapped up in woollen jacket. Sweating freely.

				No.	Surface Temperature of thigh.				No.
									after operation, 97° at 10 p.m.
29	M	46	2·5	89·5	52	48	91·4 89·6	94·1 95·45	Saline. R.T. 101·6° at 8 p.m., 3½ hours after operation.
65	M	23	3·44	93·2	23	18	—	—	
24b	M	65	9·25	90·5	33	31	—	—	
80b	M	39	2·5	89·6	24	22	—	—	
95	M	9	6·55	87·8	45	40	—	—	Mouth temp. 102·2°.
1b	F	11	4·3	88·7	26	24	—	—	
99	F	21	0·6	—	23	20	—	—	"Open ether."
67b	F	18	5·65	—	22	19	—	—	"Open ether."

LIST

OF

GENTLEMEN EDUCATED AT GUY'S HOSPITAL

WHO HAVE PASSED THE

EXAMINATIONS OF THE SEVERAL UNIVERSITIES, OR OBTAINED OTHER DISTINCTIONS, DURING THE YEAR 1914.

University of London.

Degree of Doctor of Medicine.

H. L. Hopkins | R. Montgomery

Degree of Master in Surgery.

H. Gardiner | V. Glendining

Degrees of Bachelor of Medicine and Bachelor in Surgery.

T. I. Bennett	W. M. Lansdale	O. R. L. Wilson
J. B. Dunning	W. E. Tanner	C. Witts
H. W. Evans	A. Wells	

University of Oxford.

Degree of Doctor of Medicine.

G. H. Hunt | E. P. Poulton | F. O. Stohr

Degrees of Bachelor of Medicine and Bachelor in Surgery.

J. F. Venables

University of Cambridge.

Degree of Doctor of Medicine.

N. Mutch

Degrees of Bachelor of Medicine and Bachelor in Surgery.

P. R. Boswell	J. M. Jarvie	E. S. Taylor
N. Garrard	D. V. Pickering	

University of Durham.

Degrees of Bachelor of Medicine and Bachelor in Surgery.

H. H. Elliot | H. V. Leigh | R. P. Ninnis

Royal College of Surgeons of England.

Final Examination for the Fellowship.

F. Cook | V. Glendining | G. Maxted
H. Gardiner | J. C. Jefferson | G. T. Mullally

Royal College of Surgeons of Edinburgh.

Examination for the Fellowship.

Leonard Hirsch

Royal College of Physicians of London.

Elected to the Fellowship.

H. C. Cameron | F. G. Hopkins | J. G. Taylor

Admitted to Membership.

H. W. Barber | A. Neville Cox
T. B. Heaton | J. G. P. Phillips

Final Examination for the Conjoint Diploma of the Royal College of Physicians of London and the Royal College of Surgeons of England.

January, 1914.

E. R. Bailey | C. F. Pedley | C. Sherris
P. R. Boswell | G. B. Pritchard | M. C. Thavara
F. C. S. Broome | W. R. Pryn | F. Tooth
D. W. Jones | H. Sharpe | T. R. Trounce

April, 1914.

F. D. Annesley | M. Z. Hanafy | L. Muir Smith
C. Dean | F. W. Lawson | S. B. Venugopal
J. F. Diay | E. G. Martin | H. P. Whitworth
P. J. F. L. R. Du Vergé | P. Savage | A. Wills

July, 1914.

A. L. Anthony | C. Lambrinudi | P. D. Scott
F. A. Beattie | S. A. Liebson | A. K. Selim
H. H. Elliot | D. M. MacManus | P. L. Spalding
W. D. Galloway | C. E. Petley | T. A. Townsend
A. H. Harkness | F. Gilbert L. Scott

September, 1914.

F. B. Bull	M. de Costa	L. R. Pickett
B. Burnside	C de W. Gibb	C. H. G. Penny
P. R. Chevreau	R. W. P. Jackson	E. C. W. Starling
J. S. Cocks	H. L. Messenger	

October, 1914.

A. Abdel-Al	S. S. B. Harrison	D. C. Scott
J. E. Davies	G. W. King	J. F. H. Stallman
F. H. Dodd	W. H. Nicholls	W. A. Young

Society of Apothecaries of London.

Final Examination for the Diploma.

C. de W. Gibb	W. M. Lansdale	C. R. Smith
R. J. Hearn	A. N. Minns	J. Stephenson

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Degrees of Bachelor of Medicine and Bachelor in Surgery.

R. W. Cushing | C. H. L. Harper

University of Durham.

Degree of Doctor of Medicine.

R. C. H. Francis

Final Examination for the Conjoint Diploma of the Royal College of Physicians of London and the Royal College of Surgeons of England.

January, 1915.

C. M. Anthony
G. L. Attwater
R. B. Campion
S. W. Coffin
E. J. Cooke
H. G. Dresing
A. J. K. Drew
L. S. Fry
L. Horsley
F. E. R. Laborda
C. G. McClymont
R. C. Matson
O. G. Parry-Jones
H. L. P. Peregrine
G. A. Pratt
H. Parry Price
W. L. E. Reynolds
A. F. Rook
B. F. Sampson
N. H. W. Saw
R. Sells
C. P. Symonds
S. Wilson

April, 1915.

E. C. Cline
R. Curle
W. A. Easton
C. H. Edwards
C. C. G. Gibson
H. S. Groves
R. A. Holmes
D. R. Jones
N. E. Kendall
B. Mitra
E. C. Peers
D. O. Richards
H. Q. F. Thompson
K. Westman

July, 1915.

C. W. W. Baxter
E. Biddle
J. E. Clark
G. R. Gokharkar
J. A. C. Greene
G. D. Gripper
F. A. Knott
V. E. Lloyd
G. S. B. Long
A. D. Marston
C. H. Medlock
W. L. Partridge
A. L. Punch
K. N. Purkis
T. W. Sheldon
M. J. T. Wallis

October, 1915.

M. Chadwick
T. H. Edey
A. F. G. Guinness
J. P. Jones
E. M. Litchfield
W. G. S. Neely
W. D. Newland
A. D. Vernon-Taylor

Society of Apothecaries of London.

Final Examination for the Diploma.

R. N. Craig
R. Curle
J. B. Fairclough
L. A. J. Graham
R. A. Holmes
J. F. Mackenzie
R. Quesada-Jiménez
A. Traill

LIST

OF

GENTLEMEN EDUCATED AT GUY'S HOSPITAL

WHO HAVE PASSED THE

EXAMINATIONS OF THE SEVERAL UNIVERSITIES, OR OBTAINED OTHER DISTINCTIONS, DURING THE YEAR 1916.

University of London.

Degree of Doctor of Medicine.

R. H. Wilshaw

Degrees of Bachelor of Medicine and Bachelor in Surgery.

F. V. Bevan Brown | D. S. Graves | A. L. Punch

University of Oxford.

Degrees of Bachelor of Medicine and Bachelor in Surgery.

H. E. Bamber
W. Burridge
J. M. H. Campbell
C. Dean
A. G. East
T. E. Micklem
A. Traill
S. W. F. Underhill
H. St. H. Vertue
D. M. P. Whitcombe

University of Durham.

Degrees of Bachelor of Medicine and Bachelor in Surgery.

D. O. Richards

Royal College of Physicians of London.

Admitted to Membership.

C. P. Symonds

Royal College of Surgeons of England.

Final Examination for the Fellowship.

F. D. Saner | W. E. Tanner

Final Examination for the Conjoint Diploma of the Royal College of Physicians of London and the Royal College of Surgeons of England.

January, 1916.

K. L. Bates	V. R. Hirsch	A. H. Taymour
E. S. Bowes	J. Gaymer Jones	

April, 1916.

H. J. Bensted	D. H. A. Galbraith
I. R. R. Brogden	P. G. McEvedy

July, 1916.

A. M. Ahmad	G. E. Kidman	I. Tewfik
R. Aspinall-Stivala	E. C. de M. Morgan	R. R Traill
P. D. Chapman	E. S. Phillips	W. J. Vance
L. S. Gathergood	R. L. Portway	H. S. Wacher
B. E. Jerwood	R. H. C. Pryn	

October, 1916.

J. A. M. Alcock	A. W. A. Davies	F. N. Sidebotham
H. E. Bamber	J. E. E. de Robillard	G. E. L. Simons
J. A. Berry	G. W. Heckels	H. Sterne Howitt
J. F. Carter Braine	E. A. Levis-ur	S. Vidot
	C. L. Odam	

Society of Apothecaries of London.

Final Examination for the Diploma.

W. Burridge	H. M. Gray	L. A. B. Moore
H. N. Eccles	H. T. Lamb	M. B. M. Tweed
E. Norman Glover	A. L. Malabre	H. St. H. Vertue

LIST

OF

GENTLEMEN EDUCATED AT GUY'S HOSPITAL

WHO HAVE PASSED THE

EXAMINATIONS OF THE SEVERAL UNIVERSITIES, OR OBTAINED OTHER DISTINCTIONS, DURING THE YEAR 1917.

University of London.

Degree of Doctor of Medicine.

D. J. Munro | P. Smith

Degree of Master in Surgery.

W. E. Tanner

Degrees of Bachelor of Medicine and Bachelor in Surgery.

F. Caldecott | C, S. L. Roberts | P. Smith
F. A. Knott | B Sampson

University of Oxford.

Degrees of Bachelor of Medicine and Bachelor in Surgery.

C. W. W. Armstrong | W. Gover
J. J. Conybeare | R. T. F. D. Roberts

University of Cambridge.

Degree of Master in Surgery.

A. M. Zamora

Royal College of Surgeons of England.

Final Examination for the Fellowship.

A. M. Zamora

Final Examination for the Conjoint Diploma of the Royal College of Physicians of London and the Royal College of Surgeons of England.

January, 1917.

A. T. Dabbous	F. R. Leblanc	C. R. Smith
T. L. Heath	J. A. Martin	J. G. Stevens
M. C. Joynt	M. Pearson	

April, 1917.

E. W. Bowell	L. Gill	H. N. Pritchett
O. St. L. Campion	J. C. C. Howe	W. J. Walters
	G. R. Hubbard	

July, 1917.

H. D. Apergis	H. W. Eddison	C. H. Laver
E. H. Bryant	J. W. H. Grice	N. H. S. Maelzer
W. B. Buer	S. S. M. Jabir	S. Riddiough
A. B. Cocker	H. H. Khan	J. Victory

October, 1917.

N. A. H. Barlow	J. S. Ellis	N. Kamchorn
A. Bulleid	J. C. Gie	R. C. W. Staley
J. R. Cox	D. V. Halstead	K. M. Woodruff
	E. C. Hinde	

Society of Apothecaries of London.

Final Examination for the Diploma.

E. F. Deacon | B. Ramirez

MEDALLISTS AND PRIZEMEN,

JULY, 1915.

Open Scholarships in Arts.

Edward Emile Delisle Gray, St. Paul's School, £50,
Myles Wheeler-O'Bryen, Oratory School, Edgbaston, £50, } Equal.

Open Scholarships in Science.

Albert Ernest Sawday, Prelim. Sci. Class, Guy's Hospital, £120.
Sydney Anselm Sharpe, Prelim. Sci. Class, Guy's Hospital, £50.

Scholarship for University Students.

John Maurice Hardman Campbell, B.A., New College, Oxford, £75.

Open Scholarships in Dental Mechanics.

October, 1914. **Alfred Herbert Bowes**, £20.
May, 1915. **Harold John Powell**, £20.

Scholarships in Dental Mechanics for Pupils of Guy's Hospital.

October, 1914. **Wyndham Brookes Farrington**, £20.
May, 1915. **George Frederick Faustmann**, £20.

Junior Proficiency Prizes.

Eric Clark Hinde, £30.
Francis Caldecott, £15.
Felix Raoul Leblanc, £10.
Edwin Frank Deacon, Certificate.

The Beaney Prize for Pathology.

Denys Mavesyn Percival Whitcombe, £34.

The Michael Harris Prize for Anatomy.

Francis Caldecott, }
Eric Clark Hinde, } Equal.

The Wooldridge Memorial Prize for Physiology.

Eric Clark Hinde, £10.
Edwin Frank Deacon, Certificate.
Francis Caldecott, Certificate.

Dental Prizes.

First Year's Prize in Dental Subjects.

Arthur Llewellyn Spencer Payne, £10.
Alfred Herbert Bowes, Certificate.
Clifford Andrew Loveluck, Certificate.

Second Year's Prize in General Subjects.

Frederic Harry Wallace, £10.
Petrus Lafras van Schalkwijk, Certificate.

Prize for Operative Dental Surgery.

George Dee,
Pierre Jean Hugo, } Equal.
Richard John Gustavus Halden, Certificate.

Newland-Pedley Gold Medal for Practical Dentistry.

Willem Jacobus Rousseau Viljoen.

Treasurer's Gold Medal for Clinical Medicine.

Arthur Lisle Punch.

MEDALLISTS AND PRIZEMEN,

JULY, 1916.

Open Scholarships in Arts.

Harold John Selby, Cheltenham College, £100.
Kenneth Herbert Hugh-Jones, Bradford College. £50.

Open Scholarships in Science.

Edward Henry Roche, Prelim. Sci. Class, Guy's Hospital, £120.
Reginald Cyril Bell Ledlie, Prelim. Sci. Class, Guy's Hospital, Certificate.

Scholarships for University Students.

Charles Walter Wylde Armstrong, B.A., St. John's College, Oxford, £75.
Harold George Burford, B.A., Christ Church, Oxford, £35.

Open Scholarship in Dental Mechanics.

May, 1916. Arthur Frederick Bartle, £20.

Scholarships in Dental Mechanics for Pupils of Guy's Hospital.

October, 1915. Edwin Spencer Goodwin, £20.
May, 1916. Richard Stanislaus Roche, £20.

Newland-Pedley Gold Medal for Practical Dentistry.

Richard John Gustavus Halden, Medal.
Alfred Herbert Bowes, Certificate.

Treasurer's Gold Medal for Clinical Medicine.

Edwin Seymour Phillips, Medal.
John Maurice Hardman Campbell, Proxime Accessit.

Treasurer's Gold Medal for Clinical Surgery.

Joseph Edouard Evariste de Robillard, Medal.
Leslie Somerville Gathergood, Proxime Accessit.

MEDALLISTS AND PRIZEMEN,

JULY, 1917.

Open Scholarship in Arts.

John Alexander Currie, Diocesan College, Rondebosch, £100.

Open Scholarship in Science.

Alan McKenzie, Prelim. Sci. Class, Guy's Hospital, £120.

Scholarships for University Students.

William Gover, B.A., Balliol College, Oxford, £75.
Robert Blake Poole Lansdown, B.A., Pembroke College, Cambridge, £35,

Open Scholarships in Dental Mechanics.

October, 1916.	Allistair Hyland Grieve, £10,	Equal.
	William Wallace Harold Truscott, £10,	
May, 1917.	Edric Frank Wilson, £20.	

Treasurer's Gold Medal for Clinical Medicine.

Arthur Bulleid.

Treasurer's Gold Medal for Clinical Surgery.

Leonard Snowden Debenham, Medal.
Francis Caldecott, Certificate.
José Victory, Certificate.

THE PHYSICAL SOCIETY.*

Honorary President.

Honorary Vice-Presidents.—Sir George Savage, M.D., Sir Frederick Taylor, Bart., M.D., Charters J. Symonds, M.S.

Presidents.

Hon. Secretaries.—G. T. Mullally, M.B., B.S., and T. B. Heaton, M.B., B.C.

This Society is the representative of the old Guy's Physical Society founded in the year 1771.

At eight o'clock on alternate Saturday and Wednesday evenings during the Winter Session papers are read by Students on medical or allied subjects, and a discussion follows.

At the end of each Session a Prize to the value of £10 is awarded to the Member who is judged to have read the best paper before the Society. A similar Prize of the value of £5 is awarded to the Member who has most distinguished himself in the debates, and a Prize of the value of £5 is awarded to the Member who exhibits the best specimens of scientific interest.

The Treasurer gives annually a Prize of £5 for the best essay on some set subject. The successful Essay is read at the last Meeting of the Session.

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* Since the outbreak of War the meetings of this Society have been very infrequent.

CLINICAL APPOINTMENTS HELD DURING THE YEAR 1914.

HOUSE PHYSICIANS.

W. R. Reynell	J. A. Ryle	A. C. Clifford
A. J. Eagleton	E. D. Scott	H. C. Rook
E. S. Taylor	A. Wills	

HOUSE SURGEONS.

A. Seabrooke	O. G. Morgan	E. S. Taylor
H. W. Evans	C. H. Gould	W. H. Ogilvie
A. B. Danby	E. W. Blake	

ASSISTANT HOUSE SURGEONS.

C. H. Gould	L. B. Stringer	N. Garrard
E. D. Scott	J. F. Venables	F. V. Bevan-Brown
E. W. Blake	W. E. Tanner	C. Sherris
P. R. Boswell	C. S. L. Roberts	C. F. Pedley
C. Lambrinudi	L. Muir Smith	C. Dean
P. D Scott	W. H. Ogilvie.	P. H. Berry
J. R. Barrow-Clough	R. P. Ninnis	

OUT-PATIENT OFFICERS.

A. C. Clifford	H. P. Whitworth	C. S. L. Roberts
E. S. Taylor	H. W. Evans	A. J. E. Smith
H. C. Rook	C. H. Gould	W. H. Ogilvie
F. V. Bevan-Brown	E. D. Scott	E. W. Blake
P. R. Boswell	A. B. Danby	C. Sherris
	W. E. Tanner	

OBSTETRIC RESIDENTS.

C. H. G. Pochin	F. C. S. Broome	N. Garrard
J. F. Venables	A. Seabrooke	J. F. H. Stallman

OPHTHALMIC HOUSE-SURGEONS.

H. Mather	T. A. Townsend

CLINICAL ASSISTANTS.

P. H. Berry	F. V. Bevan Brown	E. W. Blake
C. Sherris	W. E. Tanner	J. F. Venables
J. R. Barrow-Clough	P. R. Boswell	J. York Moore
C. F. Pedley	C. S. L. Roberts	H. Sharpe
C. Dean	F. E. Laborda	C. Lambrinudi
L. Muir Smith	P. D Scott	H. P. Whitworth
S. Wilson	H. L. Peregrine	L. R. Broster

CLINICAL ASSISTANTS IN THE MEDICAL WARDS.

A. S. Erulkar	C. H. L. Harper	L. Muir Smith
F. G. L. Scott	H. P. Whitworth	A. N. Minns
H. L. P. Peregrine	F. H. Dodd	O. G. Parry-Jones
H. G. Dresing	N. H. W. Saw	P. D. Scott
A. H. Taymour	H. H. Elliot	H. Parry-Price
W. M. Lansdale	H. L. Messenger	L. R. Pickett
B. Burnside	T. W. Sheldon	R. Sells
R. Curle	R. A. Holmes	E. J. Cooke

CLINICAL ASSISTANTS IN THE SURGICAL WARDS.

J. R. Barrow Clough	H. L. Messenger	W. D. Galloway
J. S. Cocks	R. W. P. Jackson	S. S. B. Harrison
D. C. Scott	T. H. Edey	D. O. Richards
N. H. W. Saw	G. A. Pratt	A. J. Drew

DRESSERS IN THE THROAT, EAR, CHILDREN'S, AND GENITO-URINARY DEPARTMENTS.

R. W. P. Jackson	A. K. Day-Lewis	L. S. Fry
A. J. Drew	T. A. Townsend	C. Dean
C. H. Medlock	H. P. Whitworth	W. R. Pryn
F. L. Spalding	C. P. Symonds	E. J. Cooke
A. F. Rook	S. W. Coffin	R. A. Holmes
J. E. Clark	C. W. W. Baxter	K. N. Purkis
V. R. Hirsch	E. Biddle	

DRESSERS IN THE THROAT, EAR, SKIN, AND ORTHOPÆDIC DEPARTMENTS.

J. F. Stallman	D. H. Galbraith	H. N. W. Saw
F. W. Lawson	R. Quesada	H. S. Groves
C. C. G. Gibson	F. C. S. Broome	B. Sampson
J. F. MacKenzie	M. Chadwick	C. Coxon
M. J. T. Wallis	W. L. Partridge	J. G. Stevens
L. H. B. Evans	G. B. Tarring	F. A. Knott
	G. L. Attwater	

DRESSERS IN THE EYE AND NERVOUS SYSTEM DEPARTMENTS.

H. F. T. Hogben	W. L. E. Reynolds	H. Q. F. Thompson
F. E. Laborda	B. Burnside	D. C. Scott
H. H. Elliot	D. McManus	L. Muir Smith
E. W. Bowell	C. Lambrinudi	H. L. P. Peregrine
N. E. Kendall	L. R. Broster	F. D. Annesley
C. R. Smith	A. L. Punch	G. S. B. Long
W. A. Young	C. E. Petley	J. Stephenson
C. de W. Gibb	K. Westman	V. E. Lloyd

SURGEONS' DRESSERS.

R. A. Holmes
G. B. Tarring
S. W. Coffin
C. C. G. Gibson
G. D. Gripper
E. J. Cooke
A. Ascher
A. L. Punch
V. R. Hirsch
C. H. Edwards
H. M. Gray
E. Biddle
A. W. Cocking
A. D. Marston
E. S. Bowes
R. Curle
E. W. Bowell
M. Chadwick
A. C. M. Coxon
C. P. Symonds
N. E Kendall
C. W. W. Baxter
J. E. Clark
J. A. Ryle
L. H. B. Evans
V. E. Lloyd
A. F. G. Guinness
A. G. East
H. Lamb
D. M. P. Whitcombe
E. M. Litchfield
K. L. Bates
W. A. Easton
W. L. Partridge
B. Sampson
L. R. Broster
A. F. Rook
M. J. T. Wallis
J. G. Stevens
G. S. B. Long
F. A. Knott
D. H. A. Galbraith
K. N. Purkis
G. Noott
W. D. Newland
A. Traill

ASSISTANT SURGEONS' DRESSERS.

J. J. Conybeare
K. N. Purkis
E. Biddle
D. H. A. Galbraith
N. H. S. Maelzer
E. M. Litchfield
J. Totton
W. D. Newland
I. R. R. Brogden
W. H. A. Pratt
K. N. Woodruff
G. E. L. Simons
J. de Robillard
F. A. Knott
J. G. Jones
L. H. B. Evans
G. Noott
A. F. G. Guinness
A. D. Marston
E. S. Bowes
A. G. East
P. G. McEvedy
W. G. S. Neely
H. J. Bensted
R. L. Portway
W. B. Buer
J. F. Mackenzie
C. H. Edwards
V. R. Hirsch
A. Traill
A. W. Cocking
E. C. de M. Morgan
L. P. Waghorn
J. B. Fairclough
D. M. P. Whitcombe
E. N. Glover
H. S. Wacher
W. J. Vance
D. V. Halstead

DENTAL SURGEONS' DRESSERS.

H. L. P. Peregrine
G. L. Attwater
B. Burnside
H. Q. F. Thompson
C. Dean

OBSTETRIC DRESSERS AND EXTERNS.

J. H. Parry
J. E. Davies
A. L. Anthony
O. G. Parry-Jones
A. S. Liebson
K. Westman
W. L. Partridge
J. S. Cocks
H. Q. F. Thompson
A. F. Rook
R. A. Holmes
K. L. Bates
E. W. Bowell
C. W. W. Baxter
G. B. Tarring
C. H. Edwards
J. F. Mackenzie
W. A. Young
W. H. Nicholls
R. W. Cushing
C. E. Petley
J. Stephenson
D. O. Richards
W. A. Easton
A. K. Day-Lewis
H. L. Messenger
M. Chadwick
R. Curle
R. W. P. Jackson
E. J. Cooke
B. Sampson
G. S. B. Long
M. J. T. Wallis
A. L. Punch
L. A. J. Graham
L. R. Pickett
A. H. Harkness
L. Horsley
C. de W. Gibb
R. J. Quesada
W. L. E. Reynolds
L. S. Fry
C. C. G. Gibson
J. F. H. Stallman
L. R. Broster
N. E. Kendall
S. W. Coffin
J. G. Stevens
J. E. Clark
G. D. Gripper

MEDICAL WARD CLERKS AND POST-MORTEM CLERKS.

C. W. W. Baxter
J. Kyle
V. E. Lloyd
L. P. Waghorn
A. D. Marston
E. M. Litchfield
A. Traill
E. A. Leveseur
J. J. Conybeare
L. H. B. Evans
V. R. Hirsch
E. Biddle
C. H. Laver
P. G. McEvedy
I. R. R. Brogden
J. B. Fairclough
A. G. East
W. J. Vance
D. V. Halstead
N. A. H. Barlow
P. D. Chapman
H. I. Sterne-Howitt
J. S. Ellis
A. Ahmad

J. Victory
J. G. Stevens
M. J. T. Wallis
G. S. B. Long
J. F. Carter Braine
M. Pearson
D. M. Whitcombe
A. G. East
F. A. Knott
G. Noott
K. N. Purkis
J. G. Jones
W. H. A. Pratt
R. L. Portway
H. S. Wacher
M. Pearson
G. E. L. Simons
H. M. Gray
E. S. Phillips
L. S. Gathergood
I. Tewfik
B. E. Jerwood
G. E. Kidman
A. L. Punch

J. E. Clark
E. S. Bowes
A. W. Cocking
A. F. G. Guinness
R. S. Craig
E. C. de M. Morgan
N. H. S. Maelzer
C. H. Edwards
D. H. A. Galbraith
V. E. Lloyd
G. B. Dowling
W. G. S. Neely
A. Bulleid
G. B. Tarring
W. D. Newland
E. N. Glover
H. J. Bensted
M. B. M. Tweed
M. C. Joynt
T. Micklem
H. W. Eddison
F. N. Sidebotham
K. R. Traill

SURGICAL WARD CLERKS.

P. J. McEvedy
A. Bulleid
C. T. Helsham
E. N. Glover
H. J. Bensted
H. Sterne Howitt
R. Aspinall-Stivala
E. S. Phillips
B. E. Jerwood
R. R. Traill
J. S. Ellis
H. E. Bamber
N. L. Watt
J. M. H. Campbell
W. Burridge

I. R. R. Brogden
C. H. Laver
H. M. Gray
J. A. Alcock
E. de Robillard
M. C. Joynt
M. B. M. Tweed
S. Vidot
G. E. Kidman
F. N. Sidebotham
H. W. Eddison
H. S. Vertue
C. L. Odam
T. L. Heath
A. W. A. Davies

J. Victory
W. H. A. Pratt
H. J. Leviseur
K. M. Woodruff
T. E. Micklem
A. M. Ahmad
I. Tewfik
N. H. Barlow
P. D. Chapman
L. S. Gathergood
G. W. Heckels
R. S. Millar
J. W. H. Grice
J. T. T. Forbes

DENTAL APPOINTMENTS HELD DURING THE YEAR 1914.

DENTAL HOUSE SURGEONS.

W. K. Fry	J. S. Palmer	R. H. Rix
H. O. Salt	M. G. Whitten	D. Clewer
M. Pearson		

ASSISTANT DENTAL HOUSE SURGEONS.

G. L. Cutts	H. J. Edwards	M. G. Whitten
S. E. Johnson	J. M. Barnes	P. E. Jessop
W. E. Coe	F. E. Welton	J. A. S Wright
P. T. Pearce	P. E. Bernhard	L. H. Cross

CLINICAL ASSISTANTS IN THE CONSERVATION ROOM.

A. E. Lowein (6 weeks)	P. E. Jessop	P. T. Pearce
J. A. S. Wright (6 weeks)	C. A. E. Cook	W. J. R. Viljoen
L. H. Cross	W. G. Hollands	F. E. Rudd
H. Curtis	G. Dee	R. G. Wilshere

ASSISTANT DEMONSTRATORS IN DENTAL MECHANICS.

C. A. E. Cook	W. J. R. Viljoen	G. Dee
	K. M. K. Duff	

ASSISTANT DEMONSTRATORS IN DENTAL METALLURGY.

G. Dee	F. J. Ordish	H. L. Thorn
	F. H. Wallace	

ASSISTANT DEMONSTRATORS IN DENTAL MICROSCOPY.

T. D. Corke	J. A. S. Wright

DRESSERS IN THE GAS ROOM.

J. W. Beacock	A. H. Cole	W. C. Hammond-Williams
L. P. Richards	J. E. Wright	
V. R. Dyke	M. G. Henry	D. A. Bevis
A. C. Dean	F. E. Welton	R. J. Pickett
F. E. Rudd	C. A. E. Cook	H. V. Stebbings
D. G. Pearce	P. T. Pearce	S. A. Withers
M. G. Whitten	A. E. Lowein	W. G. Hollands
J. A. S. Wright	W. E. Coe	T. D. Corke
W. G. Lloyd	G. W. Wheldon	J. L. Mugford
W. J. McB. Allan	E. A. Dawson	L. Machin
D. F. Small	F. D. Neal	J. A. Johnstone
E. C. Lewis	J. J. S. Hill	R. J. Ryland
J. M. Barnes	E. G. Browne	P. E. Jessop
O. N. Mash	P. E. Bernhard	P. L. van Schalkwijk
F. H. Wallace	C. F. Hawkins	G. Deeks
W. J. R. Viljoen	H. V. Vogt	G. H. Danks
C. R. Martin	J. L. Garrard	P. R. C. Martin

DRESSERS IN THE EXTRACTION ROOM.

F. J. Ordish
F. H. Wallace
J. Alcee
G. H. Danks
C. M. Bullpitt
C. F. Hawkins
M. G. Watson
W. G. Hollands
W. D. Penfold
F. C. Lean
G. A. Pennant
M. C. V. Thom
C. R. Martin
H. M. S. Pillow
R. J. G. Handel
G. W. Allen
S. J. Peatfield

G. C. Williamson
K. M. K. Duff
W. J. Viljoen
N. Allen
C. R. Martin
H. L. Thorn
H. V. Vogt
J. J. L. Hollington
C. Bethencourt
P. R. C. Martin
R. G. Wilshere
L. A. Morris
H. Curtis
G. Deeks
C. H. Kidner
O. O. Lloyd
B. Eady

S. G. Smith
G. Dee
C. S. Southwell
H. P. Parkes
E. P. Deverall
W. P. Barfoot
L. G. Whelpton
A. H. Bevan
A. A. Osman
G. F. H. Bloom
L. R. J. Hallett
P. J. Hugo
S. A. Wolf
G. M. Thomas
H. Muir Smith
C. F. Curle
M. H. Wermig

CASUALTY DRESSERS.

R. C. Brough
S. A. Withers
J. J. Hollington
W. J. R. Viljoen
P. L. van Schalkwijk
E. G. Browne
A. C. Bullpitt
M. G. Watson
P. R. C. Martin
G. Dee
G. H. F. Bloom
C. S. Southwell
E. P. Deverall
C. L. Curle

T. D. Corke
J. A. S. Wright
G. W. Wheldon
N. Allen
F. H. Wallace
H. Curtis
H. P. Parkes
G. H. Howe
S. G. Smith
G. M. Thomas
C. R. Martin
W. P. Barfoot
F. C. Lean
O. O. Lloyd

L. Machin
E. A. Dawson
L. H. Cross
E. H. Bryant
J. L. Oates
G. Deeks
C. F. Hawkins
H. V. Vogt
C. R. Cade
R. G. Wilshere
L. A. Morris
G. H. Danks
G. W. Allen

CLINICAL APPOINTMENTS HELD DURING THE YEAR 1915.

HOUSE PHYSICIANS.

E. D. Scott	L. Muir-Smith	R. C. Holmes
A. Wills	R. W. P. Jackson	B. Burnside
C. H. L. Harper	C. Dean	
C. P. Symonds	G. L. Attwater	

HOUSE SURGEONS.

W. H. Ogilvie	P. R. Boswell	S. Wilson
A. B. Danby	W. E. Tanner	J. F. H. Stallman
E. W. Blake	C. Lambrinudi	D. O. Richards
C. H. Gould	P. D. Scott	N. E. Kendall

ASSISTANT HOUSE SURGEONS.

G. L. Attwater	R. Curle	A. L. Punch
H. L. P. Peregrine	D. O. Richards	J. E. Clark
E. J. Cooke	C. W. W. Baxter	A. Traill
S. Wilson	C. H. Medlock	
N. E. Kendall	G. D. Gripper	

OUT-PATIENT OFFICERS.

P. R. Boswell	L. R. Broster	N. E. Kendall
C. S. L. Roberts	G. L. Attwater	D. O. Richards
W. E. Tanner	C. H. Edwards	A. Traill
P. D. Scott	J. F. H Stallman	C. W. W. Baxter
L. Muir-Smith	S. Wilson	C. H. Medlock
C. Dean	B. Burnside	A. L. Punch
C. Lambrinudi	R. Curle	

OBSTETRIC RESIDENTS.

J. F. H. Stallman	B. Burnside	A. D. Marston
A. Seabrooke	R. A. Holmes	
A. F. Rook	C. F. Pedley	

OPHTHALMIC HOUSE SURGEONS.

T. A. Townsend	R. Sells	F. A. Knott

CLINICAL ASSISTANTS.

G. D. Gripper	J. Gaymer Jones	H. M. Gray
R. Quesada	V. R. Hirsch	J. G Stevens
C. H. Medlock	C. W. W. Baxter	
D. H. A. Galbraith	D. M. P. Whitcombe	

CLINICAL ASSISTANT IN THE MEDICAL WARDS.

E. C. Cline

CLINICAL ASSISTANTS IN THE SURGICAL WARDS.

D. H. A. Galbraith
H. Q. F. Thompson
A. H. Taymour
D. O. Richards
J. G. Stevens
V. R. Hirsch
A. D. Marston

DRESSERS IN THE THROAT, EAR, AND GENITO-URINARY DEPARTMENTS, AND CLERKS IN THE CHILDREN'S DEPARTMENT.

G. Noott
J. Gaymer Jones
I. R. R. Brogden
E. S. Bowes
P. G. McEvedy
D. V. Halstead
F. N. Sidebotham
G. E. Kidman
B. E. Jerwood
T. E. Micklem

DRESSERS IN THE THROAT, EAR, AND ORTHOPÆDIC DEPARTMENTS, AND CLERKS IN THE SKIN DEPARTMENT.

A. W. Cocking
W. H. A. Pratt
E. M. Litchfield
S. Wacher
W. J. Vance
W. B. Buer
R. L. Portway
R. H. C. Pryn
G. E. L. Simons
P. D. Chapman
N. H. S. Maelzer
D. V. Halstead

DRESSERS AND CLERKS IN THE DEPARTMENTS FOR DISEASES OF THE EYES, AND OF THE NERVOUS SYSTEM.

M. C. Joynt
R. R. Traill
E. N. Glover
H. Sterne Howitt
K. M. Woodruff
A. Traill
W. D. Newland
J. E. Clark
A. H. Taymour
C. W. W. Baxter
G. E. L. Simons
H. J. Bensted
H. M. Gray.

OBSTETRIC DRESSERS AND EXTERNS.

V. R. Hirsch
K. N. Purkis
E. M. Litchfield
L. H. B. Evans
A. G. East
V. E. Lloyd
E. S. Bowes
E. Biddle
F. A. Knott
A. D. Marston
D. H. A. Galbraith
H. M. Gray
W. D. Newland
P. G. McEvedy
J. Gaymer Jones
A. Traill
J. Kyle
G. Noott
W. H. A. Pratt
H. E. Bamber
E. N. Glover
K. M. Woodruff
D. M. P. Whitcombe
M. Pearson
I. R. R. Brogden
A. M. Ahmad
W. Burridge
E. C. de M. Morgan
M. B. M. Tweed
E. S. Phillips
H. J. Bensted
I. Tewfik
L. S. Gathergood
R. L. Portway

EXTERNS ONLY.

W. G. S. Neely | A. F. G. Guinness.

MEDICAL WARD AND POST-MORTEM CLERKS.

E. N. Glover
K. M. Woodruff
R. H. C. Pryn
H. S. Wacher
W. B. Buer
M. Pearson
D. V. Halstead
R. L. Portway
G. E. L Simons
W. J. Vance
H. J. Bensted
T. E. Micklem
I. Tewfik
R. R. Traill
W. G. S. Neely
F. N. Sidebotham
L. S. Gathergood
P. D. Chapman
A. F. G. Guinness
E. S. Phillips
E. A. Leviseur
A. M. Ahmad
H. I. Sterne-Howitt
D. M. P. Whitcombe
G. E. Kidman
M. C. Joynt
B. E. Jerwood
H. E. Bamber
R. S. Millar
S. Vidot
J. E. de Robillard
T. L. Heath
A. W. A. Davies
W. Burridge
G. W. Heckels
J. M. H. Campbell
H. St. H. Vertue
C. L. Odam
M. B. M. Tweed
J. T. T. Forbes
S. W. F. Underhill
O. St. L. Campion
J. O. R. Montocchio
V. Ramirez
J. C. C. Howe
R. Aspinall-Stivala
N. A. H. Barlow.
J. W. H. Grice
J. Victory
L. A. B. Moore
L. Gill
E. H. Bryant
H. D. Apergis
E. F. Deacon
E. C. Hinde
F. R. Leblanc
H. N. Pritchett
G. R. Hubbard
J. A. M. Alcock
J. A. Berry
W. J. Walters
W. R. G. Hearnden
C. G. Coombs
J. R. Cox
A. Magill
S. T. Wong
W. A. Hawes
J. C. Gie
S. M. M. Jabir
F. J. Harrington
G. H. Fitzgerald

SURGEONS' DRESSERS.

M. B. M. Tweed
T. E. Micklem
J. S. Ellis
H. M. Gray
W. H. A. Pratt
D. M. P. Whitcombe
G. E. Kidman
P. G. McEvedy
I. R. R Brogden
F. N. Sidebotham
K. M. Woodruff
E. N. Glover
W. B. Buer
H. S. Wacher
D. V. Halstead
M. Pearson
W. Burridge
R. L. Portway
H. J. Bensted
G. E. L. Simons
W. J. Vance
H. I. Sterne-Howitt
N. H. S. Maelzer
T. E. Micklem
R. R. Traill
E. S. Phillips
E. A. Leviseur
L. S. Gathergood
A. M. Ahmad
P. D. Chapman
B. E. Jerwood
R. H. C. Pryn
I. Tewfik
M. C. Joynt
A. W. A. Davies
J. T. T. Forbes
E. de Robillard
J. F. Carter Braine
G. W. Heckels
C. L. Odam
J. A. M. Alcock
L B. Moore
T. L. Heath
S. Vidot
J. M. H. Campbell
H. St. H. Vertue
H. E. Bamber

ASSISTANT SURGEONS' DRESSERS.

R. R. Traill
B. E. Jerwood
J. T. MacManus
M. C. Joynt
E. S. Phillips
A. Roca
H. Sterne-Howitt
P. D. Chapman
L. S. Gathergood
I. Tewfik
E. A. Leviseur
C. L. Odam
R. S. Millar
G. W. Heckels
A. W. A. Davies
S. Vidot
J. T. T. Forbes
H. St. H. Vertue
H. E. Bamber
T. L. Heath
J. M. H. Campbell
R. H. C. Pryn
R. Aspinall-Stivala
J. O. R Montocchio
B. Ramirez
J. C. C. Howe
L. B. Moore
S. W. F. Underhill
O. St. L. Campion
E. F. Deacon
F. R. Leblanc
W. J. Walters
J. A. Berry
L. Gill
H. D. Apergis
E. H. Bryant
H. N. Pritchett
G. R. Hubbard

SURGICAL WARD CLERKS.

L. B. Moore	F. R. Leblanc	J. C. Gie
W. J. Walters	E. H. Bryant	C. W. W. Armstrong
J. O. R. Montocchio	G. R. Hubbard	T. Fernandez
B Ramirez	H. D. Apergis	A. Y. Massouda
O. St. L. Campion	S. M. M Jabir	L. S. Debenham
J. C. C. Howe	S. T. Wong	F. Caldecott
S. W. F. Underhill	A. Magill	R. C. W. Staley
G. A. Pennant	J. R. Cox	N. Kamchorn
G. W. Pratt	W. A. Hawes	F. W. Reitz
E. F. Deacon	W. R. G. Hearnden	H. Millett
E. C. Hinde	C. G. Coombs	O. Halstead

STUDENT DEMONSTRATORS OF MICROSCOPICAL PATHOLOGY.

R. A. Holmes	E. N. Glover	J. E. Clark
F. R. Leblanc		

DENTAL SURGEONS' DRESSER.

C. W. W. Baxter

ASSISTANT SURGEONS' CLERK.

F. Caldecott

OUT-PATIENT CLERKS.

H. G. Burford | W. H. Grace

PATHOLOGICAL ASSISTANT TO THE DEMONSTRATORS OF MORBID ANATOMY.

D. M. P. Whitcombe

STUDENT DEMONSTRATOR OF ANATOMY.

W. H. Grace

DENTAL APPOINTMENTS HELD DURING THE YEAR 1915.

DENTAL HOUSE SURGEONS.

W. E. Coe	H. O. Salt	F. E. Rudd
J. M. Barnes	L. H. Cross	W. J. R. Viljoen
A. E. Lowein	E. E. Johnson	

ASSISTANT DENTAL HOUSE SURGEONS.

L. S. Pilbeam	C. R. Martin	R. G. Wilshere
C. F. Hawkins	S. Gordon Smith	C. H. Kidner
H. L. Thorn	B. Eady	O. O. Lloyd
C. L. Curle	G. M. Thomas	P. J, Hugo

CLINICAL ASSISTANTS IN THE CONSERVATION ROOM.

F. C. Lean	C. H. Kidner	A. H. Bowes
B. Eady	O. O. Lloyd	P. Green
S. A. Woolf	L. H. Dixon	

ASSISTANT DEMONSTRATORS OF DENTAL MECHANICS.

S. A. Woolf	S. Sanders	P. Green
L. H. Dixon		

ASSISTANT DEMONSTRATORS OF DENTAL METALLURGY.

A. H. Bowes	S. Sanders	A. L. S. Payne

DRESSERS IN THE GAS ROOM.

L. H. Cross	C. F. Hawkins	H. L. Thorn
S. Gordon Smith	W. J. R. Viljoen	C. M. Bullpitt
C. L. Curle	M. G. Watson	L. A. Morris
H. Curtis	M C. V. Thom	C. S. Southwell
E. C. Lewis	E. P. Deverall	A. S. Blacklaws
C. S. Southwell	R. J. G. Halden	L. H. Dixon
G. Dee	G. H. Danks	W. A. Cooper
G. Deeks	O. O. Lloyd	W. P. Barfoot
C, R. Martin	G. W. Allen	W. Mercer
G. M. Thomas	P. J. Hugo	A. H. Bowes
R. G. Wilshere	C. H. Kidner	H. Muir-Smith
E. A. Dawson	C R. Cade	J. A. S. Wright
P. R. C. Martin	S. A. Woolf	S. Sanders
H. V. Vogt	G. F, H. Bloom	

CASUALTY DRESSERS.

P. J. Hugo	A. S. Blacklaws	E. T. Crosoer
M. C. V. Thom	W. A. Cooper	R. L. Cowley
C. H. Kidner	L. H. Dixon	R. K. Gundlach
S. A. Woolf	A. H. Bowes	H. L. Ide
B. Eady	P. Green	W. R. Wotton
R. J. G, Halden	W. Mercer	D. E. Robinson
H. Muir-Smith	S. Sanders	
S. J. Peatfield	P. H. Marsh	

DRESSERS IN THE ORDINARY EXTRACTION ROOM.

H. O. Long	R, L. Cowley	S, G. Townley
S. Sanders	P. H. Marsh	E. W, Jarvis
A. S. Blacklaws	D. E. Robinson	H. J. Powell
P. Green	R. K. Gundlach	H. O. Irwin
W. A. Cooper	W. Mercer	L. D. Crabb
L. H. Dixon	C. A. Lovelock	A. Weinberg
F. K. Escritt	H. Muir-Smith	L. F. Fouraker
A. L. S. Payne	H. L. Ide	G. F. Faustmann
F. C. Lean	W. R. Wotton	F. R. Salsbury
G. W. Allen	W. A. Cooper	A. F. Percy
E. T. Crosoer	W. P. Barfoot	
A. H. Bowes	F. G. P. Flanders	

CLINICAL APPOINTMENTS HELD DURING THE YEAR 1916.

HOUSE PHYSICIANS.

G. L. Attwater	A. L. Punch	A. H. Taymour
R. A. Holmes	C. W. W. Baxter	E. S. Phillips
B. Burnside	J. E. Clark	L. S. Gathergood
C. Dean	F. A. Knott	T. E. Micklem

HOUSE SURGEONS.

J. F. H. Stallman	C. H. Medlock	P. G. McEvedy
D. O. Richards	R Curle	I. R. R. Brogden
N. E. Kendall	A. D. Marston	E. S. Bowes
S. Wilson	K. L. Bates	R. R. Traill

ASSISTANT HOUSE SURGEONS.

A. Traill	I. Tewfik	F. N. Sidebotham
J. E. Clark	H. S. Wacher	H. E. Bamber
J. Gaymer-Jones	B. E. Jerwood	H. Sterne-Howitt
V. R. Hirsch	L. B. Moore	
R. Quesada	G. E. L. Simons	

OUT-PATIENT OFFICERS.

C. W. W. Baxter	A. D. Marston	T. E. Micklem
R. Curle	A. Abdel-Al	R. R. Traill
C. H. Medlock	I. R. R. Brogden	J. F. Carter-Braine
A. L. Punch	P. G. McEvedy	G. W. Heckels
K. L. Bates	A. H. Taymour	E. de Robillard
J. E. Clark	E. S. Bowes	H. St. H. Vertue
F. A. Knott	L. S. Gathergood	

OBSTETRIC RESIDENTS.

A. D. Marston	S. Wilson	R. Quesada
C. Lambrinudi	D. O. Richards	H. S. Wacher
E. S. Bowes	C. H. Medlock	

OPHTHALMIC HOUSE SURGEONS.

F. A. Knott	J. F. H. Stallman	S. Wilson

CLINICAL ASSISTANTS.

H. E. Bamber	G. Noott	J. F. Carter-Braine
E. A. Leviseur	F. N. Sidebotham	M. C. Joynt
K. M. Woodruff	J. A. M. Alcock	
B. E. Jerwood	E. de Robillard	

CLINICAL ASSISTANTS IN THE SURGICAL WARDS.

M. Pearson | W. Burridge | M. C. Joynt

DRESSERS IN THE THROAT, EAR, AND GENITO-URINARY DEPARTMENTS, AND CLERKS IN THE CHILDREN'S DEPARTMENT.

H. Sterne-Howitt
S. Vidot
G. E. L. Simons
M. C. Joynt
H. E. Bamber

C. L. Odam
T. L. Heath
J. C. C. Howe
S. W. F. Underhill
H. T. Lamb

A. Bulleid
J. R. Cox
J. C. Gie
C. H. Laver

DRESSERS IN THE THROAT, EAR, AND ORTHOPÆDIC DEPARTMENTS, AND CLERKS IN THE SKIN DEPARTMENT.

G. W. Heckels
W. Burridge
R. S. Millar

A. W. A. Davies
J. T. T. Forbes
M. Pearson

F. J. Harrington

DRESSERS AND CLERKS IN THE DEPARTMENTS FOR DISEASES OF THE EYES AND OF THE NERVOUS SYSTEM.

I. Tewfik
E. de Robillard
R. H. C. Pryn
L. S. Gathergood
D. V. Halstead
J. O. R. Montocchio
A. M. Ahmad
R. S. Millar

J. M. H. Campbell
P. D. Chapman
G. W. Heckels
S. M. M. Jabir
C. L. Odam
J. J. Conybeare
H. St. H. Vertue
W. Burridge

J. A. Berry
O. St. L. Campion
L. Gill
E. H. Bryant
W. R. G. Hearnden
L. H. B. Evans
W. J. Walters
G. R. Hubbard

OBSTETRIC DRESSERS AND EXTERNS.

P. D. Chapman
T. E. Micklem
R. R. Traill
E. A. Leviseur
J. M. H. Campbell
H. St. H. Vertue
G. E. Kidman
B. E. Jerwood
F. N. Sidebotham
N. H. S. Maelzer
J. F. Carter-Braine
W. J. Vance
H. S. Wacher
O. St. L. Campion
A. W. A. Davies
J. T. T. Forbes
E. de Robillard

H. S. Wacher
W. J. Walters
H. W. Eddison
D. V. Halstead
G. W. Heckels
M. C. Joynt
C. L. Odam
R. H. C. Pryn
G. E. L. Simons
H. Sterne-Howitt
T. L. Heath
R. Aspinall-Stivala
J. S. Ellis
E. H. Bryant
E. F. Deacon
J. C. C. Howe
S. W. F. Underhill

H. N. Pritchett
G. R. Hubbard
F. J. Harrington
J. A. Berry
L. Gill
R. Leblanc
R. S. Millar
B. Ramirez
J. J. Conybeare
J. W. H. Grice
S. T. Wong
C. G. Coombs
E. C. Hinde
S. M. M. Jabir
F. G. T. Lewtas
A. Magill

OBSTETRIC DRESSERS ONLY.

H. D. Apergis | N. A. H. Barlow | J. O. R. Montocchio

EXTERN ONLY.

E. F. Deacon

MEDICAL WARD AND POST-MORTEM CLERKS.

J. A. M. Alcock
L. B. Moore
E. H. Bryant
L. Gill
E. C. Hinde
J. A. Berry
E. F. Deacon
W. J. Walters
H. N. Pritchett
F. R. Leblanc
J. R. Cox
W. A. Hawes
A. Magill
C. G. Coombs
S. T. Wong
W. R. G. Hearnden
A. Bulleid
C. H. Laver
J. C. Gie
G. R. Hubbard
H. D. Apergis
G. H. FitzGerald
T. Fernandez
N. Kamchorn
R. C. W. Staley
W. A. Flynn
O. Halstead

G. A. S. Shacklock
C. W. W. Armstrong
G. Meadows
J. W. H. Grice
A. Y. Massouda
B. C. W. Simpson
H. G. Burford
F. Caldecott
H. J. Leviseur
W. H. Steavenson
A. R. Doyle
A. L. S. Payne
A. A. Osman
S. Wolff
H. O. Long
F. W. Reitz
J. Victory
L. S. Debenham
W. H. Grace
H. Millett
A. G. M. Severn
C. R. Cade
F. Young
C. G. Siggs
H. F. G. Berncastle
F. K. Escritt
C. Gill-Carey

C. Moffatt
A. R. Neckles
A. G. Ord
G. V. Richards
S. H. Robinson
W. H. Simmons
W. Skelly
G. M. Thomas
J. E. de V. van der Merwe
C. L. Curle
J. Joffe
E. F. Kerby
E. H. L. LeClezio
S. A. Withers
W. Gover
W. Kilroe
R. T. F. D. Roberts
E. R. Webb
G. R. Aspinwall
T. G. D. Bonar
W. H. Cellier
G. Hume
L. Lyne
G. F. Peters
R. S. Ralph
R. W. Warrick

POST-MORTEM CLERK ONLY.

S. M. M. Jabir

SURGEONS' DRESSERS.

S. W. F. Underhill
N. A. H. Barlow
B. Ramirez
G. R. Hubbard
H. D. Apergis
J. O. R. Montocchio
J. C. C. Howe
O. St. L. Campion
L. Gill
J. A. Berry
F. J. Harrington
E. F. Deacon
F. R. Leblanc

J. W. H. Grice
S. M. M. Jabir
E. H. Bryant
H. N. Pritchett
E. C. Hinde
C. G. Coombs
C. H. Laver
A. Magill
J. R. Cox
S. T. Wong
A. Bulleid
L. S. Debenham
J. Victory

J. C. Gie
W. R. G. Hearnden
H. Millett
N. Kamchorn
G. Meadows
F. Caldecott
G. A. S. Shacklock
R. C. W. Staley
W. A. Flynn
A. Y. Massouda
C. W. W. Armstrong
T. Fernandez
O. Halstead

ASSISTANT SURGEONS' DRESSERS.

A. Magill
J. R. Cox
F. J. Harrington
C. H. Laver
J. C. Gie
W. A. Hawes
C. G. Coombs
W. R. G. Hearnden
S. M. M. Jabir
A. Bulleid
S. T. Wong
G. H. FitzGerald
H. W. Eddison
L. S. Debenham
H. Millett
O. Halstead
G. A. S. Shacklock
W. A, Flynn
F. Caldecott
F. W. Reitz
R. C. W. Staley
N. Kamchorn
B. C. W. Simpson
A. Y. Massouda
C. W. W. Armstrong
J. Victory
T. Fernandez
G. Meadows
H. G. Burford
W. H. Grace
S. Wolff
A. R. Doyle
A. L. S. Payne
A. G. M. Severn
H. O. Long
W. H. Steavenson
C. R. Cade
H. J. Leviseur
A. A. Osman
H. F. G. Berncastle
W. Kilroe
G. V. Richards
W. Skelly
S. A. Withers
F. K. Escritt
J. Joffe
R. D. Roberts
C. G. Siggs
J.E.deV.van der Merwe
C. Gill-Carey
E. F. Kerby
E. H. L. LeClezio
A. R. Neckles
W. H. Simmons
C. L Curle
W. Gover
C. Moffatt
G. M. Thomas
E. R. Webb

SURGICAL WARD CLERKS.

W. H. Grace
F. Young
A. R. Doyle
A. G. M. Severn
C. G. Siggs
S. Wolff
H. G. Burford
H. O. Long
A. L. S. Payne
C. R. Cade
W. H. Steavenson
A. A. Osman
C. L. Curle
St. G. B. D. Gray
E. H. L. LeClezio
S. A. Withers
A. G. Ord
E. R. Webb
W. H. Simmons
S. H. Robinson
A. R. Neckles
W. Skelly
E. F. Kerby
J. E. de V. van der Merwe
C. Gill-Carey
C. Moffatt
G. M. Thomas
J. Joffe
F. K. Escritt
W. Kilroe
H. F. G. Berncastle
T. G. D. Bonar
R. W. Warrick
G. R. Aspinwall
R. G. Mayer
W. H. Cellier
L. Lyne
R. S. Ralph
G. F. Peters
C. C. Bennett
L. Lavine
W. H. Southgate
G. A. A. Bradnack
N. E. Kendall
H. M. Brown
C. H. Horwitz
K. Mullen

OUT-PATIENT CLERKS.

St G. B. D. Gray
C. C. Bennett
W. Skelly
E. R. Webb
G. F. Peters
R. S. Ralph
W. H. Simmons
S. A. Withers
R. W. Warrick
B. M. Tonkin
T. G. D. Bonar
H. W. Southgate

PATHOLOGICAL ASSISTANTS TO THE DEMONSTRATORS OF MORBID ANATOMY.

G. W. Heckels
C. L. Odam
J. Joffe
E. H. L. LeClezio

STUDENT DEMONSTRATORS OF MICROSCOPICAL PATHOLOGY.

G. W. Heckels | C. W. W. Armstrong

STUDENT ASSISTANT IN THE BACTERIOLOGICAL DEPARTMENT.

W. Gover

DENTAL APPOINTMENTS HELD DURING THE YEAR 1916.

DENTAL HOUSE SURGEONS.

C. R. Martin
R. G. Wilshere
G. Dee
H. L. Thorn
B. Eady
C. H. Kidner
O. O. Lloyd
A. H. Bowes
W. A. Cooper
P. Green

ASSISTANT DENTAL HOUSE SURGEONS.

S. A. Woolf
G. W. Allen
W. Mercer
A. H. Bowes
P. H. Marsh
E. T. Crosoer
W. A. Cooper
L. H. Dixon
S. G. Townley
D. E. Robinson
F. G. P. Flanders
W. R. Wotton
H. J. Powell

CLINICAL ASSISTANTS IN THE CONSERVATION ROOM.

R. L. Cowley
E. T. Crosoer
P. H. Marsh
H. J. Powell
S. G. Townley
H. O. Irwin
S. C. Turner
F. R. Knowler
H. M. Marshall

ASSISTANT DEMONSTRATORS OF DENTAL MECHANICS.

G. Wilshere
R. S. Roche

ASSISTANT DEMONSTRATORS OF DENTAL METALLURGY.

D. E. Robinson
W. A. Woodward

DRESSERS IN THE GAS ROOM.

F. C. Lean
C. H. Kidner
P. J. Hugo
M. H. Wermig
A. H. Bowes
L. H. Dixon
P. H. Marsh
W. R. Wotton
D. E. Robinson
P. Green
H. Wallis
F. R. Salsbury
S. Sanders
P. H. Marsh
B. Eady
S. G. Townley
G. W. Allen
H. L. Ide
R. J. G. Halden
R. L. Cowley
H. O. Irwin
A. S. Blacklaws
O. O. Lloyd
C. C. Becker
G. F. Faustmann
E. T Crosoer
C. Bethencourt
L. D. Crabb
F. G. P. Flanders
H. J. Powell
J. E. Fishburn
P. J. S. de Wet
G. Wilshere
P. E. Grobbelaar
S. G. Townley
E. F, Shaw
W. Mercer
H. Ll. Jones
K C. Brough
J. C. Johnson

CASUALTY DRESSERS.

F. R. Salsbury
S. G. Townley
C. C. Becker
G. F. Faustmann
H. O. Irwin
H. J. Powell
A. Weinberg
E. F. Shaw
A. F. Percy
J. C. Johnson
P. E. Grobbelaar
H. Ll. Jones
F. R. Knowler
L. D. Crabb
F. G. P. Flanders
H. M. Marshall
S. C. Turner
J. E. Fishburn
M. B. Burton
P. J. S. de Wet
G. Wilshere
T. Barton
H. Fox
E. A. P. Parker
W. A. Woodward
A. N. Goudge
W. D. Hatton
R. V. Kingham

DRESSERS IN THE ORDINARY EXTRACTION ROOM.

C. C. Becker
H. O. Irwin
G. Wilshere
E. F. Shaw
H. J. Powell
G. F. Faustmann
J. C. Johnson
H. Ll. Jones
F. R. Knowler
F, R. Salsbury
P. J. S. de Wet
A. N. Goudge
S. E. Tweney
R. V. Kingham
E. A. P. Parker
L. M. Wheeler
W. A. Woodward
T. A. M. Wilson
P. E. Grobbelaar
M. B. Burton
H. M. Marshall
S. C Turner
W. D. Hatton
B. M. Tonkin
H. Fox
A. B. Aldred
T. Barton
R. S. Roche
K. C. Brough
J. E. Fishburn
G. H. Danks
L. D. Crabb
A. Maher
A. F. Bartle
F. L. King
M. Ginsberg
H. O. Holmes
W. H. Turner
R. M. Underwood
J. L. Lean

CLINICAL APPOINTMENTS HELD DURING THE YEAR 1917.

HOUSE PHYSICIANS.

E. S. Phillips	M. Pearson	J. J. Conybeare
L. S. Gathergood	O. St. L. Campion	D. V. Halstead
T. E. Micklem	H. N. Pritchett	J. C. Gie
A. H. Taymour	H. E. Bamber	

ASSISTANT HOUSE PHYSICIANS.

J. J. Conybeare	J. W. H. Grice	W. Gover
C. G. Coombs	J. C. Gie	R. T. F. D. Roberts
J. R. Cox	J. T. T. Forbes	A. L. S. Payne
C. H. Laver	C. W. W. Armstrong	W. H. Grace
A. Bulleid	F. Caldecott	

HOUSE SURGEONS.

I. R. R. Brogden	J. G. Stevens	C. H. Laver
E. S. Bowes	H. E. Bamber	W. B. Buer
R. R. Traill	G. R. Hubbard	A. Bulleid
P. G. McEvedy	L. Gill	J. Victory
M. C. Joynt	W. J. Walters	J. R. Cox
R. Quesada	J. W. H. Grice	F. R. Leblanc

ASSISTANT HOUSE SURGEONS.

F. N. Sidebotham	G. E. L. Simons	J. T. T. Forbes
H. E. Bamber	B. Ramirez	H. J. Leviseur
H. Sterne Howitt	R. C. W. Staley	

OUT-PATIENT OFFICERS.

J. F. Carter Braine	H. E. Bamber	F. Caldecott
G. W. Heckels	T. L. Heath	R. C. W. Staley
E. de Robillard	S. M. M. Jabir	
H. St. H. Vertue	S. Riddiough	

OBSTETRIC RESIDENTS.

R. Quesada	H. S. Wacher	E. H. Bryant
C. H. Medlock	J. Victory	S. M. M. Jabir

OPHTHALMIC HOUSE SURGEONS.

S. Wilson	N. H. S. Maelzer	K. M. Woodruff.

ASSISTANT CASUALTY OFFICERS.

O. St. L. Campion	D. V. Halstead	C. G. Coombs
J. C. C. Howe	H. Millett	H. O. Long
W. J. Walters	W. B. Buer	L. S. Debenham
B. Ramirez	J. C. Gie	G. A. S. Shacklock

CLINICAL ASSISTANT.

J. J. Conybeare

CLINICAL ASSISTANT IN THE SURGICAL WARDS.

F. J. Harrington

DRESSERS IN THE THROAT AND EAR DEPARTMENTS.

L. S. Debenham
E. C. Hinde
G. Meadows
G. A. S. Shacklock
C. W. W. Armstrong
F. W. Reitz
G. H. FitzGerald
F. Caldecott
R. S. Millar
A. A. Osman
W. H. Grace
A. R. Neckles
A. L. S. Payne
S. A. Withers
J. Joffe
S. Wolff
T. D. G. Bonar
C. Gill-Carey
G. M. Thomas
J. E. de V. vander Merwe
E. F. Kerby
H. F. G. Berncastle
W. K. McKay
C. G. D. Siggs
C. G. Coombs
T. Fernandez
O. Halstead
A. Magill

CLERKS IN THE CHILDREN'S DEPARTMENT.

L. S. Debenham
E. C. Hinde
G. Meadows
G. A. S. Shacklock
A. Y. Massouda
W. H. Steavenson
A. R. Doyle
W. A. Hawes
E. H. L. Le Clezio
H. O. Long
G. R. Aspinwall
W. H. Cellier
F. W. Reitz

DRESSERS IN THE GENITO-URINARY DEPARTMENT.

L. S. Debenham
E. C. Hinde
G. Meadows
G. A. S. Shacklock
J. Joffe
S. Wolff
F. Caldecott
R. S. Millar
A. A. Osman
H. F. G. Berncastle
W. K. McKay
C. G. D. Siggs

CLERKS IN THE SKIN DEPARTMENT.

C. G. Coombs
T. Fernandez
O. Halstead
A. Magill
H. G. Burford
L. S. Debenham
J. C. Gie
N. Kamchorn
W. Gover
G. Meadows
G. V. Richards
R. D. Roberts
F. Caldecott
G. A. S. Shacklock
F. K. Escritt
C. Moffatt
A. A. Osman
W. H. Simmons
G. H. FitzGerald

DRESSERS IN THE ORTHOPÆDIC DEPARTMENT.

C. G. Coombs
T. Fernandez
O. Halstead
A. Magill
C. W. W. Armstrong
F. W. Reitz
G. H. FitzGerald
W. H. Grace
A. R. Neckles
A. L. S. Payne
S. A. Withers
T. G. D. Bonar
C. Gill-Carey
G. M. Thomas
J. E. de V. vander Merwe
E. F. Kerby

CLERKS IN THE DEPARTMENT FOR DISEASES OF THE NERVOUS SYSTEM.

W. A. Flynn
H. N. Pritchett
R. C. W. Staley
H. D. Apergis
N. A. H. Barlow
S. T. Wong
H. G. Burford
J. C. Gie
N. Kamchorn
W. Gover
G. Meadows
G. V. Richards
R. D. Roberts
G. A. S. Shacklock
F. K. Escritt
C. Moffatt
A. A. Osman
A. H. Simmons
G. H. FitzGerald
F. Caldecott
L. S. Debenham

DRESSERS IN THE EYE WARDS.

W. A. Flynn
H. D. Apergis
N. A. H. Barlow
S. T. Wong
H. N. Pritchett
R. C. W. Staley
A. Y. Massouda
W. H. Steavenson
L. S. Debenham
J. C. Gie
N. Kamchorn
A. R. Doyle
W. A. Hawes
E. H. L. Le Clezio
H. O. Long
W. Gover
G. Meadows
G. V. Richards
R. D. Roberts
F Caldecott
G. A. S. Shacklock
G. R. Aspinwall
W. H. Cellier
F. W. Reitz
F. K. Escritt
C. Moffatt
A. A. Osman
W. H. Simmons
G. H. FitzGerald
H. G. Burford

OBSTETRIC DRESSERS AND EXTERNS.

C. W. W. Armstrong
J. R. Cox
W. R. G. Hearnden
A. Y. Massouda
H. Millett
J. Victory
A. Bulleid
F. Caldecott
J. C. Gie
N. Kamchorn
C. H. Laver
H. J. Leviseur
J. T. T. Forbes
W. Gover
W. H. Grace
W. A. Hawes
H. O. Long
G. Meadows
A. L. S. Payne
R. D. Roberts
A. R. Doyle
T. Fernandez
W. A. Flynn
O. Halstead
A. G. M. Severn
R. C. W. Staley
G. A. S. Shacklock
H. G. Burford
C. L. Curle
L. S. Debenham
G. M. Thomas
F. W. Reitz
J. E. de V. van der Merwe
C. Gill-Carey
W. H. Steavenson
H. F. G. Berncastle
F. K. Escritt
C. Moffatt
A. A. Osman
C. G. D. Siggs
W. H. Simmons
E. F. Kerby
H. P. Barker
E. H. L. Le Clezio
A. R. Neckles
G. F. Peters
S. A. Withers
J. Joffe
R. Gainsborough
R. S. Ralph
G. V. Richards
R. W. Warrick
S. Wolff

SURGEONS' DRESSERS.

W. Gover
R. D. Roberts
A. G. M. Severn
A. R. Doyle
C. Moffatt
A. A. Osman
F. W. Reitz
H. G. Burford
A. L. S. Payne
S. Wolff
W. H. Grace
W. A. Hawes
H. O. Long
C. L. Curle
J. Joffe
G. V. Richards
H. F. G. Berncastle
F. K. Escritt
G. M. Thomas
J. E. de V. van der Merwe
C. Gill-Carey
A. R. Neckles
W. H. Simmons
S. A. Withers
E. F. Kerby
E. H. L. Le Clezio
C. G. D. Siggs
P. J. Briggs
W. G. Hay
G. F. Peters
R. S. Ralph
G. R. Aspinwall
S. H. Robinson
R. Gainsborough
K. M. K. Duff
C. V. Brown
M. F. Ismail
H. N. Schapiro
R. W. Warrick
W. H. Steavenson
T. G. D. Bonar
W. H. Cellier
R. B. P. Lansdown
C. H. Horwitz
K. Mullen
L. Lyne
H. M. Brown
G. B. Dowling
S. H. Robinson
J. Kendall
A. G. Ord
W. H. Southgate
G. Hume
E. R. Webb
R. C. B. Ledlie
F. Young

MEDICAL WARD AND POST-MORTEM CLERKS.

G. H. FitzGerald
E. F. Kerby
A. R. Neckles
G. V. Richards
H. F. G. Berncastle
C. G. Siggs
W. H. Simmons
C. L. Curle
F. K. Escritt
G. M. Thomas
S. A. Withers
C. Gill-Carey
J. Joffe
J. E. de V. van der Merwe
G. R. Aspinwall
R. S. Ralph
T. G. D. Bonar
S. H. Robinson
C. Moffatt
R. W. Warrick
W. H. Cellier
G. F. Peters
G. B. Dowling
G. A. A. Bradnack
H. M. Brown
K. Mullen

E. R. Webb
C. H. Horwitz
L. Lyne
G. Hume
J. Kendall
H. W. Southgate
W. R. Carling
W. G. Hay
M. F. Ismail
L. Lavine
H. Le Vieux
S. T. Barrett
C. V. Brown
A. K. Day Lewis
G. Massie
C. H. St. John
C. R. Cade
E. E. D. Gray
C. T. Helsham
H. N. Schapiro
C. C. Bennett
P. J. Briggs
I. R. Florence
R. B. P. Lansdown
A. M. Mishad
H. S. Morris
H. Ameen

J. G. Barrie
J. V. C. Braithwaite
W. Mark Brown
L. Burvill-Holmes
M. Cohen
W. T. Flooks
E. E. D. Gray
R. C. B. Ledlie
G. Massie
W. W. Payne
T. Reed
G. R. Reeves
S. Rose
A. E. Sawday
B. M. Tonkin
J. E. Wright
S. Cohen
G. L. Cutts
K. M. K. Duff
G. P. Lindsay
E. T. Lloyd
D. J. O'Meara
C. M. Probert
N. V. Wadsworth
W. H. Turner
G. H. Howe

ASSISTANT SURGEONS' DRESSERS.

W. H. Cellier
G. B. Dowling
E. H. L. Le Clezio
R. S. Ralph
G. F. Peters
T. G. D. Bonar
G. R. Aspinwall
R. W. Warrick
J. Kendall
R. Mullen
I. R. Florence
C. H. Horwitz

H. M. Brown
L. Lyne
H. W. Southgate
E. R. Webb
G. A. Bradnack
G. Hume
L. Lavine
S. T. Barrett
I. R. Florence
A. M. Mishad
H. Ameen
J. G. Barrie

S. Rose
J. V. C. Braithwaite
M. Cohen
L. Burvill-Holmes
A. E. Sawday
W. T. Flooks
B. M. Tonkin
J. E. Wright
W. Mark Brown
W. W. Payne
G. K. Reeves

SURGICAL WARD CLERKS.

S. T. Barrett
P. J. Briggs
K. M. K. Duff
R. B. P. Lansdown
H. S. Morris
C. V. Brown
W. G. Hay
M. F. Ismail
H. N. Schapiro
A. M. Mishad
L. Burvill-Holmes
R. C. B. Ledlie
A. E. Sawday
W. Mark Brown
G. K. Reeves

K. M. K. Duff
H. Ameen
J. G. Barrie
M. Cohen
E. E. D. Gray
W. W. Payne
C. H. St. John
B. M. Tonkin
G. A. Piper
S. Rose
J. E. Wright
J. V. C. Braithwaite
W. T. Flooks
G. Massie
D. J. O'Meara

N. V. Wadsworth
S. Cohen
E. T. Lloyd
W. H. Summerskill
E. P. Wilson
I. B. McCann
H. Le Vieux
G. P. Lindsay
G. L. Cutts
T. W. Turner
E. C. Grey
M. S. Mahmud
M. A. R. Khalifa
W. A. Turner

PATHOLOGICAL ASSISTANTS TO THE DEMONSTRATORS OF MORBID ANATOMY.

L. S. Debenham | T. G. D. Bonar | H. W. Southgate

STUDENT DEMONSTRATORS OF MICROSCOPICAL PATHOLOGY.

J. Victory | L. S. Debenham | M. Cohen

ASSISTANT SURGEONS' CLERKS.

J. Herbert	M. S. Mahmud	G. E. W. Felce
H. S. Morris	W. H. Turner	P. L. Richardson
M. A. R. Khalifa	M. Maizels	W. H. Summerskill

DENTAL SURGEON'S DRESSER.

R. S. Millar

STUDENT ASSISTANT IN THE BACTERIOLOGICAL DEPARTMENT.

C. H. St. John

STUDENT DEMONSTRATOR OF ANATOMY.

G. Massie

DENTAL APPOINTMENTS HELD DURING THE YEAR 1917.

DENTAL HOUSE SURGEONS.

A. H. Bowes	L. H. Dixon	H. Ll. Jones
W. A. Cooper	F. G. P. Flanders	
P. Green	H. J. Powell	

ASSISTANT DENTAL HOUSE SURGEONS.

E. F. Shaw	M. B. Burton	A. F. Bartle
J. C. Johnson	H. M. Marshall	P. J. S. de Wet
H. O. Irwin	S. C. Turner	F. R. Knowler

CLINICAL ASSISTANTS IN THE CONSERVATION ROOM.

A. F. Bartle | F. L. King

ASSISTANT DEMONSTRATOR OF DENTAL MECHANICS.

A. H. Grieve

ASSISTANT DEMONSTRATORS OF DENTAL METALLURGY.

J. James | R. M. Underwood

DRESSERS IN THE GAS ROOM.

F. G. P. Flanders
R. V. Kingham
H. Fox
S. C. Turner
C. C. Becker
K. C. Brough
A. N. Goudge
E. A. P. Parker
W. D. Hatton
R. M. Underwood
M. B. Burton
F. R. Knowler
H. M. Marshall
S. E. Tweney
G. Wilshere
A. F. Bartle
R. S. Roche
A. Maher
F. L. King
T. Barton
S. G. Townley
E. T. Crosoer
H. J. Powell
A. Ll. Jones
M. Ginsberg
P. J. S. de Wet
H. O. Holmes
E. F. Shaw
S. C. Turner
P. E. Grobbelaar
J. C. Johnson
E C. Keet
P. J. Morrison
W. W. H. Truscott
W. A. Woodward
C. L. D. Pasmore
E. G. Foulston
J. James
I. M. Thomson
J. Alcée
J. Lauer

DRESSERS IN THE ORDINARY EXTRACTION ROOM.

W. H. Turner
J. James
L. D. Crabb
C. L. D. Pasmore
H. M. Marshall
E. G. Foulston
H. O. Holmes
W. W. H. Truscott
A. Maher
S. V. White
F. L. King
E. C. Keet
P. J. Morrison
H. Fox
R. M. Underwood
M. Ginsberg
A. H. Grieve
I. M. Thomson
J. Herbert
J. L. Lean
E. Samuels
J. Lauer
S. H. Coplans
C. P. Lake
J. W. Greenwall
J. E. Fisburn
D. C. van der Spuy
D. W. Smale Adams
A. B. Ford
I. Bitar
C. C. de A. Birch

CASUALTY DRESSERS.

A. F. Bartle
A. Maher
R. S. Roche
M. Ginsberg
F. L. King
E. G. Foulston
A. N. Goudge
S. E. Tweney
H. Fox
M. B. Burton
R. V. Kingham
H. Ll. Jones
E. A. P. Parker
P. E. Grobbelaar
P. J. S. de Wet
W. A. Woodward
W. D. Hatton
S. C. Turner
J. E. Fishburn
H. M. Marshall
H. J. Powell
H. O. Holmes
J. James
J. L. Lean
J. Alcée
F. R. Knowler
P. J, Morrison
C. L. D. Pasmore
W. W. H. Truscott
J. C. Johnson
R. M. Underwood
E. F. Shaw
G. Wilshere
J. W. Greenwall
S, H. Coplans
I. M. Thomson

GUY'S HOSPITAL.

MEDICAL AND SURGICAL STAFF.

1917.

Consulting Physicians.—Sir Frederick Taylor, Bart., M.D.; G. Newton Pitt, M.D.; Sir E. Cooper Perry, M.D.; W. Hale White, M.D.

Consulting Surgeons.—W. H. A. Jacobson, M.Ch.; C. H. Golding-Bird, M.B.; Charters J. Symonds, M.S.; Sir W. Arbuthnot Lane, Bart., M.S.

Consulting Physician for Mental Diseases.—Sir George Savage, M.D.

Consulting Ophthalmic Surgeon.—C. Higgens, Esq.

Consulting Dental Surgeons.—F. Newland-Pedley, Esq.; W. A. Maggs, Esq.

Consulting Anæsthetists.—Tom Bird, Esq.; H. F. Lancaster, M.D.; C. J. Ogle, Esq.

Physicians and Assistant Physicians.

L. E. Shaw, M.D.	A. F. Hurst, M.D.
J. Fawcett, M.D.	H. C. Cameron, M.D.
A. P. Beddard, M.D.	G. H. Hunt, M.D.
H. S. French, M.D.	E. P. Poulton, M.D.

Surgeons and Assistant Surgeons.

L. A. Dunn, M.S.	R. P. Rowlands, M.S.
Sir Alfred Fripp, M.S., C.B., K.C.V.O.	P. Turner, M.S.
	E. C. Hughes, M.Ch.
F. J. Steward, M.S.	R. Davies-Colley, M.Ch
C. H. Fagge, M.S.	L. Bromley, M.Ch.

Obstetric Surgeons.

G. Bellingham Smith, M.B., B.S.	H. Chapple, M.Ch.

Ophthalmic Surgeons.

H. L. Eason, M.S., M.D.	A. W. Ormond, Esq.

Surgeons in Charge of Throat and Ear Department.

W. M. Mollison, M.Ch.	T. B. Layton, M.S.

Surgeon in Charge of Actino-Therapeutic Department.
C. E. Iredell, M.D.

Surgeon in Charge of the Orthopædic Department.
W. H. Trethowan, M.S.

Surgeon in Charge of the Genito-Urinary Department.
A. R. Thompson, Ch.M.

Physician in Psychological Medicine.
Maurice Craig, M.D.

Physician in Charge of Skin Department.
Sir E. Cooper Perry, M.D.

Physician in Charge of the Department for Nervous Diseases.
A. F. HURST, M.D.

Physician in Charge of the Department for Diseases of Children.
H. C. CAMERON, M.D.

Dental Surgeons.
R. WYNNE ROUW, ESQ. | M. F. HOPSON, ESQ.
H. L. PILLIN, ESQ. | J. B. PARFITT, ESQ.

Assistant Dental Surgeons.
J. L. PAYNE, ESQ. | F. J. PEARCE, ESQ.
E. B. DOWSETT, ESQ. | H. C. MALLESON, ESQ.

Resident Dental Officer.
F. BOCQUET BULL, ESQ.

Anæsthetists.
G. ROWELL, ESQ. | F. E. SHIPWAY, M.D.
H. M. PAGE, ESQ. | A. M. ZAMORA, M.Ch.
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